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CIVILIAN MEDICAL DEFENSE AND ITS ADAPTATION TO PEACETIME CIVIL LIFE*

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BOSTON

OUR normal way of living has been greatly upset, and we have gradually been adjusting ourselves to new conditions forced on us as a nation and as individuals as the result of a war not of our own choosing. We have been forced into a war by enemies who were quite sure that we, as a nation, could not get together in time to avoid defeat. They considered us selfish, stupid and soft because we lived at peace with our neighbors, respected the rights of others, and were unprepared to meet and repel their sneaking attack upon us. Perhaps we were a bit blind to the dangers threatening us, but somehow it is not in our make-up to attribute to any human being such low qualities as we have found our enemies to possess!

Be that as it may, we have swung into line in a manner characteristic of our way of doing things. Once we began, nothing was allowed to stand in the way of accomplishing the end toward which all our efforts were directed. That end is quite some way off as yet, but all of us and all our allies know that the ultimate end is victory for us. And — our enemies of the Axis know it, but do not as yet admit it — out loud!

The thought comes to mind, however, in all this hard struggle and increasing sacrifice, of what is going to happen when the final victory is won and we once again return to our peaceful manner of living. Shall we again lapse into our former error of assuming that all nations can be trusted to carry out their signed covenants? Are we going to forget the lessons we have learned the hard way? Are we going to allow the work done in setting up the medical organization of the Office of Civilian Defense to go to seed and fail to profit by it in the future just because peace has returned? I do not believe so — any more than we should disband our police force just because no murder had been committed recently or there had been no riots for some time.

Before the Office of Civilian Defense was created, the only adequately organized disaster setup was the American Red Cross, but even it would have considerable difficulty in handling any sudden large-scale enemy action against us. This threat is spurring us on to get ready for the time when enemy action will strike this country, and should continue to drive us to perfect our civilian defenses. The threat has by no means been removed as yet, and may be even more imminent and nearer than we think. As the enemy becomes more desperate and despairing of the victory that they assumed to be certain for themselves, they may readily resort to action against our shores in an attempt to intimidate us and bolster their own failing morale. The work to perfect our civilian defense has been no small task, and the magnitude of it can be somewhat appreciated when one realizes that practically every community in the country has organized itself to ensure, in so far as possible, the care of injured people. Property when destroyed can be restored and rebuilt. Life cannot. Death is permanent.

In the Boston night-club disaster of some six months ago, it takes but little imagination to visualize what might have happened regarding loss of life if the civilian-defense organization had not been prepared to function. Although the deaths reached the distressing number of 491, it is safe to say that this number would have been larger but for the functioning of the Emergency Medical Service. Ambulances, doctors, nurses and hospitals were available and ready to handle the injured immediately after the disaster occurred. One thing above all stands out as instrumental in saving lives — the lack of it would quite definitely have created a most serious problem, but owing to the Emergency Medical Service it was instantly avail-

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able in abundance and to spare. I refer of course to blood plasma. At the time of the disaster over 2700 units of plasma set aside for the Emergency Medical Service were instantly available in the city itself, and a total of 3564 units in the State. It is doubtful whether such a supply would have been so quickly available under peacetime conditions. This plasma was on hand largely because of the tireless efforts of those whose job it was to think and plan for a catastrophe that might strike any community. This work is being carried on, and as of April 1 of this year, sixty hospitals in New England reported a total of 23,121 plasma units in storage and immediately available.

This is just one example of why we must not allow ourselves to relapse into blissful inertia when war conditions are no longer present and a general letdown would threaten the safety of any large number of people. How much plasma would have been available in the hospitals under the old conditions is, of course, a matter of speculation; but it is doubtful whether anywhere near an adequate number of units for a disaster of this magnitude would have been on hand, although a small number of units might have been obtainable from commercial sources.

What about the hospitals and the emergency organizations they have set up? Handicapped as these hospitals are by their greatly reduced staffs and personnel, they are, nevertheless, ready to function at a moment's notice should large numbers of casualties suddenly be brought to their doors. This has been no small task of organization in the face of continually dwindling medical and nursing staffs, as well as of the other personnel so necessary for the adequate functioning of any hospital. Being forced to run a hospital with about half its usual peacetime personnel is no easy job, to say nothing of the additional difficulties in trying to maintain and replace supplies of all kinds when they are becoming more and more difficult to obtain; and yet hospital administrators and superintendents are doing just these things.

The peacetime civilian hospital organized on an emergency wartime basis has already proved itself in a serious disaster not presumably of enemy origin. This same emergency that proved the worth and wisdom of a large store of plasma also showed the value of such civilian defense efforts in hospital organization.

It may not be generally known that during the Cocoanut Grove disaster 80 per cent of the casualties were brought into the emergency wards of two hospitals at the rate of one case in every eleven seconds. One hospital received 325 casualties, another 114. It needs no great stretch of the imagination to visualize what confusion might easily have resulted had not the Emergency Medical Service been established, and through practice drills each person's role been set down and everyone made familiar with his specific duties. Shorthanded as these hospitals were, there was no confusion; and it is quite certain that because of the well-devised plan and the well-drilled organization, not a single life was needlessly sacrificed or even jeopardized.

The reserve pool of nurses that had been organized for some time was called on, and the response on the part of these retired nurses to fill in for the emergency was more than adequate for the need. They came immediately and served without question, uncomplainingly and gladly. Many worked overtime for as long as there was any need for them. The Red Cross volunteer nurses' aides swung into line, responding in large numbers to fill any position requested. The entire Red Cross setup of ambulances and canteens worked steadily, in some instances day and night—long hours for many of them.

Why do I dwell at length on this particular disaster? It is for the purpose of bringing out the point that had it not been for the Emergency Medical Service the mortality would unquestionably have been much higher.

We are learning during these strenuous times how to function adequately with greatly reduced resources. We are building up a medical organization that will function on the instant, without becoming overwhelmed by a sudden wave of casualties in spite of fewer people to handle the situation. Through practice sessions the weak points are brought out, and these can be remedied at the next field exercise. We are learning to accomplish more, in spite of having less with which to work. We are learning the true value of many things to which we have in the past given but little thought because there was always plenty more where they came from. In plain language, we are learning the hard way to be less wasteful and more appreciative and conserving of what we have. We can already make less go farther, and much to our surprise find that it works rather well.

Another factor developed by the present threatening conditions is the arrangement for mutual aid between communities and states. It is quite possible that a state could be so seriously hit by disaster that it was beyond its own resources to cope with the conditions. The resources of neighboring states are now available and ready for such an eventuality, and they can send assistance quickly with little confusion, since their own emergency resources are well known and immediately available.

The work that has gone into the development and organization of medical resources should not

be lightly cast aside when peace returns. These services, possibly in a modified form, are a valuable adjunct in the event of any catastrophe involving human lives.

The question of an adequate number of nurses for the staffing of hospitals and for the taking care of patients in their homes is a serious one. "Luxury nursing," as it may be termed, is practically a thing of the past, and there is considerable difficulty in obtaining even essential and necessary nursing care. The replacement of nurses who have entered the armed forces is becoming increasingly difficult, since the number of new applicants for training for the nursing profession is not keeping up with the number of trained nurses being withdrawn. The reasons for this are many and readily understandable, but the solution of the problem is difficult.*

The establishment of pools from which nurses can be obtained when urgently needed is of much value. Many retired nurses are willing and glad to return to work, giving as many hours as they can. A number of these same nurses are taking refresher courses in nearby hospitals to brush up on such advances in nursing as have taken place since last they were in active practice.

Physicians, retired for some time, are back at work — especially in the hospitals — and having the time of their lives at it. The term "retiring age" under the present emergency conditions is no longer a compliment. Much valuable work is being done by the older men who so gladly return to work filling the vacancies caused by the younger ones who have gone into the service. All this wartime activity stimulates us to look ahead and to prepare our medical resources so that they will be ready to function when enemy action hits us and the care of casualties is imperative.

Why run the risk of throwing away all this tremendous effort just because the threat of enemy action against us will have been removed with the return of peace? Floods, hurricanes, conflagrations and catastrophes of one kind or another will continue at intervals even in peacetime. It would be little short of criminal to allow the preparations we have made for mutual aid in caring for those whom disaster will strike under war conditions to be dissipated and forgotten when peace returns. The effort necessary to keep a civilian-defense organization going in peacetime would of course be minimal, and the knowledge, coupled with a feeling of safety, that we were prepared to meet disaster in any form would more than repay the efforts of those people farsighted enough to hold such an organization together even if only on a small scale.

*At the time this paper was presented, the United States Cadet Nurse Corps program was not under way.

This trained and disciplined group would act with greater efficiency in aiding the already existing peacetime organizations than would people hurriedly gathered together, and would provide a reservoir of manpower that could be drawn on, with the knowledge that the needs of any particular situation could be met. By being ready they could make their work more effective. The practice gained will be invaluable if the enemy strikes, and inversely, experiences gained from enemy attacks will prove profitable in peacetime disasters. Co-operation and not regimentation has always been the American way. Mutual aid as exemplified by the civilian-defense organization is a typically American way of aiding our neighbors who are in distress. This may be in a local community, within a state or in another state — it makes no difference. The war has caused us to develop and perfect an organization for mutual aid unparalleled in our history. Without the Emergency Medical Service, untold numbers would needlessly suffer and die.

The value of all this is not conjectural. We have proof, not only in England but also in our own country, in the time when civilian-defense forces have aided materially in natural disasters caused by fire and flood. The aid rendered has been so valuable that it seems neither reasonable nor possible that a thinking people would be willing to give it all up when the present emergency is over.

My closing thought and appeal is to ask you all to consider seriously the possibility that the emergency medical services in your own communities will carry on and will preserve a type of organization that could be called up at any time to save life and property and alleviate the human misery that goes hand in hand with any disaster. An emergency, anticipated and prepared for, ceases to be an emergency. It is up to us to see to it that the lessons learned from the Emergency Medical Service are not thrown away.

17 Court Street

Discussion

Dr. C. H. Parsons, Concord: Dr. Reggio's description of the value after the war of the services furnished by the Office of Civilian Defense is much to the point. However, they can be of value then only as they are adequately organized at the present time. The majority of our communities are extremely well organized. That has been proved in the several highly successful drills that have been held. The drills, however, have shown certain deficiencies, which have been due primarily to lack of attention to the details of organization and to inadequate practice.

During the summer, an attempt will be made by the state committee to aid each community in reorganizing

its medical services according to a plan that has been made necessary by the present types of bombing and by the new methods of medical care following thermal burns. This reorganization has been shown necessary by the events taking place during and after the Cocoanut Grove fire.

I am sure that the emergency medical services in the communities of New Hampshire will be adequately trained and organized to take care of any incident, should such an unhappy state of affairs occur.

DR. W. J. P. DYE, Wolfeboro: The question of civilian defense has been adequately and inspiringly covered by Dr. Reggio. A great many of us, particularly those in the smaller communities such as that from which I come, have a tendency to be optimistic about the situation. It looks as though things were rolling fairly well, and that the chances of any incidents in this country are quite small, so far as actual bombing or things of that sort are concerned; nevertheless, Dr. Reggio has mentioned that there is a possibility of nuisance bombing or some attempt to destroy civilian morale.

The entire civilian setup is, on the whole, so far as I can judge from my own and the neighboring communities, fairly well organized. A typical incident occurred in Wolfeboro not so long ago, when a large dairy farm suddenly caught fire in the early morning hours. It was in the middle of the winter, when the temperature was subzero, and the firemen worked under considerable difficulties. The motor corps and various other units were on the scene practically as soon as the firemen were, and they furnished hot coffee and gave first-aid care promptly and with a great deal of interest.

That was a small casualty in a small community. But if it is multiplied by many such casualties in large communities, such as are likely to happen in peacetime, and if we have, as Dr. Reggio has said, continued interest and continued practice in civilian-defense methods and in organization, then all these emergencies can be better met and we shall have achieved quite an advance in community and national service.

THE TREATMENT OF ANGINA PECTORIS*

A Summary of Ten Years' Objective Study

JOSEPH E. F. RISEMAN, M.D.†

BOSTON

IT IS well recognized that patients differ in their response to therapy, yet in evaluating the efficacy of treatment in angina pectoris this fact has not been taken into consideration. It is also self evident that various methods of therapy must differ considerably in value, yet there is little in the published reports or in the claims of the pharmaceutical houses to permit comparison.

Objective studies of the value of treatment in angina pectoris have been carried out in a special clinic of the Beth Israel Hospital since 1933. To date, sixty-eight different methods of chemical, physical and surgical therapy have been studied by clinical and objective procedures that permit unbiased comparison of effectiveness. Some of the results have been reported.[1-7] The detailed data of these and the unreported results are too voluminous to be presented in detail here, and will be the subject of a forthcoming monograph.

The purpose of this paper is to present a summary of these results, with special reference to variations in the response to therapy and to a practical plan of treatment with the methods most likely to be of value.

METHODS OF STUDY

The objective studies that have been carried out have been based on the following self-evident premises. First, since angina pectoris occurs only in human beings, the value of therapy must be measured in terms of patients. Secondly, since exercise is the commonest precipitating cause of attacks, any treatment to be of value must enable the patient subsequently to do more work before experiencing pain. Observations during the last ten years have shown that the value of any form of treatment can be determined objectively by measuring the amount of work that can be done before angina is induced, provided that the measurements are made under conditions closely simulating those responsible for the majority of attacks in daily life, and that they are standardized in such a manner that the response to therapy is the only variable factor that can influence the exercise tolerance.

The standardized exercise-tolerance test. Previous studies[1] have shown that several factors materially influence the amount of work that can be done by patients with angina pectoris before pain is induced (Fig. 1‡). These factors have usually been overlooked by investigators studying the exercise tolerance of such patients. The importance of exercise in the cold must be emphasized, for if patients exercise at ordinary room temperatures, approximately one third fail to develop an attack,[1, 8, 9] whereas in others the exercise tolerance varies independently of therapy. If these conditions are properly standardized, as shown in Fig-

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‡Figs. 1, 2, 4, 6 and 9 have been reproduced from the motion picture "Angina Pectoris," produced at the Beth Israel Hospital and based on these studies.

ure 2, the amount of work necessary to induce angina becomes remarkably constant (usually around 10 per cent of the average exercise tolerance).

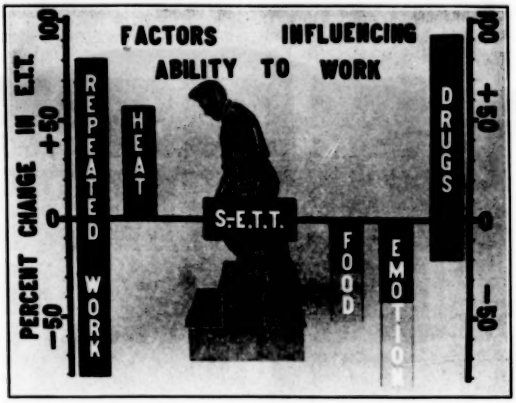

FIGURE 1.

Method of administering medication for evaluating the response to therapy. The variable course of angina pectoris makes it necessary to evaluate the effect of therapy at frequent intervals. Patients were seen in a special clinic weekly. At each visit the patient's and the physician's impressions of the clinical response to therapy were recorded, and also the number of attacks experienced since the last visit. In addition, the standardized exercise tolerance was determined one or two hours after the last dose of medication.

Several months of observation were necessary to determine the usual frequency of attacks in daily life and the usual exercise tolerance. When these had been ascertained, medication was given three or four times daily for at least a week. If there

FIGURE 2.

was no evidence of improvement, another therapeutic measure was tried. If there appeared to be a therapeutic response, a placebo resembling the drug being evaluated was given for one or two weeks or until the apparent therapeutic response disappeared. Later the studies were repeated on at least two occasions, the medication being given in disguised form — painted with tincture of cudbear, sugar coated or enclosed in a capsule.

Electrocardiographic studies gave further objective evidence that the response to therapy was not psychologic or fortuitous but was due to a positive effect on the heart. In most patients with angina pectoris, exercise causes characteristic changes in the electrocardiogram that are commonest and most striking in the precordial lead.[10] They consist of a deviation — usually a depression — of the initial portion of the RS-T segment. This begins shortly after the onset of exercise, reaches a maximum when the patient is forced to stop because of pain, and thereafter either subsides rapidly — frequently within fifteen seconds — or shows further progression, especially the height of the T waves. Because of the progressive and transient nature of the changes, the tracings must be obtained immediately after exercise, and only one lead can be observed during any one attack. The time necessary to adjust the electrodes and machine makes it impossible to obtain comparable tracings by any other technic.

Most therapeutic measures that decrease myocardial anoxia and thereby enable the patient to do more work without pain prevent or minimize the electrocardiographic changes that accompany exercise (Fig. 3).[6, 7] The degree to which these changes are prevented is an index of the therapeutic effect or potency of the medication and of the patient's response to it.

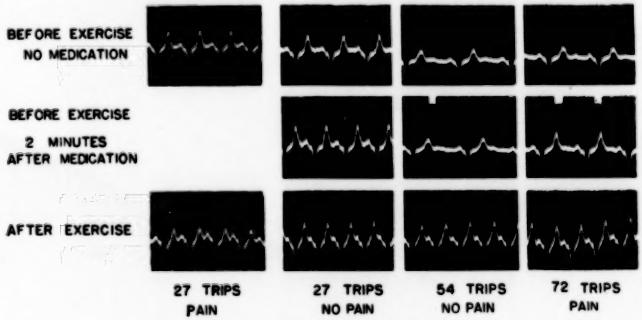

FIGURE 3. *Electrocardiograms before and after Exercise, without and with Medication (1/200 gr. nitroglycerin).*

Correlation between the results of the standardized exercise-tolerance test and the clinical response to therapy. The standardized exercise-tolerance test makes it possible to differentiate real improvement due to therapy and apparent improvement unrelated to it. Patients who show an increase in exercise tolerance of 100 per cent or more following treatment usually have complete or almost complete freedom from attacks in daily life. An increase of 30 to 75 per cent is usually associated with a moderate diminution, but not complete disappearance of these attacks. An increase of 20 per cent or less is usually unassociated with any clinical improvement.

The converse is not true. Most patients with angina pectoris feel better after visiting the physician, regardless of the therapy prescribed. Furthermore, some of those with infrequent attacks have periods of relative comfort. Without an objective test, neither patient nor physician can say whether these periods of relief are the specific result of treatment or are merely coincidental with therapy.

Shortcomings of other methods used to evaluate therapy. The inadequacy of studying the efficacy of therapy by clinical evaluation alone is apparent from the above discussion. It is not surprising that the majority of published reports indicate that a wide variety of therapeutic agents — including many that are obviously inert — are apparently of value in treating patients with angina pectoris. It must be remembered that the clinical evaluation of the benefit of therapy is, in fact, the physician's impression of the patient's opinion of the response to treatment. Objective measurements are essential.

Attempts at having the patient report the response to therapy in terms of ability to perform

such customary tasks as walking and climbing stairs are similarly misleading. Few patients invariably experience pain in daily life after a given amount of work. Such factors as environmental temperature, food, emotion, physical activity and the relation to previous attacks cannot be readily controlled or observed by the patient. Furthermore, such studies fail to reveal remissions in the course of the disease unrelated to therapy.

The electrocardiographic response to anoxia[11-13] is a valuable objective means of measuring the response to therapy, but has no close or clear-cut correlation to the clinical response. For example, nitroglycerin, the most potent drug available for the treatment of angina pectoris, does not yield such good results as does intravenous aminophyllin when measured by this method.[12] This is probably because the response to nitroglycerin occurs two or three minutes after its administration[4] and may have ceased by the time that anoxia induces changes in the electrocardiogram. The response to cobra venom is an additional illustration of the inadequacy of using the electrocardiograph in evaluating clinical response. Since this drug causes no vasodilatation, the marked clinical improvement that may occur is not associated with any electrocardiographic improvement during exercise or induced anoxia.[14]

Subjects used in the present studies. For the purpose of this summary, an analysis was made of the results in 75 patients, chosen because they had been observed for long periods of time and because their response to many different forms of medication had been measured. All patients had Heberden's angina[15] due to coronary-artery disease of arteriosclerotic origin. From 10 to 35 patients were studied in evaluating most methods of therapy. The study of larger numbers was impractical, for the evaluation of any form of therapy requires weeks or months of study, and the clinical course of patients with angina pectoris is variable and is frequently interrupted by cardiovascular accidents and the like that are unrelated to therapy. These patients' clinical course and response to therapy were known so well, however, that an accurate biologic assay was possible. In the cases in which the therapeutic procedure was hazardous — surgery — or time consuming and expensive — bed rest, x-ray therapy and so forth — fewer patients were studied. In these cases the patients selected included one or two who were known to respond favorably to several simple methods of treatment, and also one or two who were known to respond to practically no method of treatment.

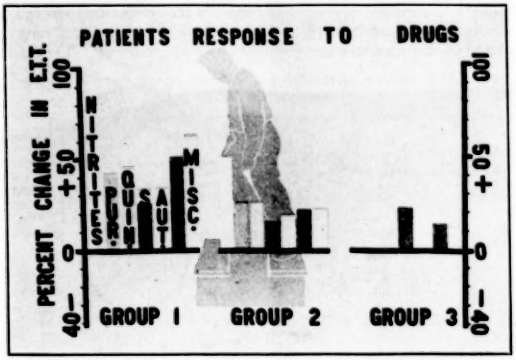

FIGURE 4.

This diagram shows the average of results in 3 patients in each of Groups 1, 2 and 3 who received nitroglycerin (nitrites), theobromine sodium acetate (purines), quinidine sulfate (quinidine), codeine sulfate (sedatives), atropine sulfate (autonomic drugs), enteric-coated potassium iodide (iodides) and locally applied heat (miscellaneous).

RESULTS

Variations in Therapeutic Response

It is possible to divide patients with angina pectoris into three groups on the basis of their

response to most therapeutic measures. Some patients, termed "marked reactors," show a striking response to practically all effective methods of therapy. Others, termed "moderate reactors," show a moderate response to the same therapeutic measures, and still others, termed "nonreactors," show little or no response to most available methods of therapy (Fig. 4).

The response to nitroglycerin can be used to determine the likelihood of response to other forms of treatment and serves to divide patients into the three groups described, as shown in Table 1.

TABLE 1. *Changes in the RS-T Segment of the Electrocardiogram during Exercise following the Administration of Nitroglycerin (1/200 gr.).*

GROUP NO.	PATIENT	BEFORE TREATMENT			TWO MINUTES AFTER TREATMENT		
		AMOUNT OF WORK NECESSARY TO INDUCE PAIN	OCCURRENCE OF PAIN	DEPRESSION OF S-T SEGMENT	AMOUNT OF WORK	OCCURRENCE OF PAIN	DEPRESSION OF S-T SEGMENT
		trips		*mm.*	*trips*		*mm.*
1	S. E.	27	Yes	2.7	27	No	0.2
	S. R.	51	Yes	2.7	51	No	0.5
	H. Schl.	54	Yes	2.5	54	No	0.4
	M. L.	40	Yes	1.8	40	No	0.0
	H. Schr.	22	Yes	1.5	22	No	0.0
	R. C.	26	Yes	1.0	26	No	0.0
2	P. R.	49	Yes	3.5	49	No	1.9
	L. W.	36	Yes	2.7	36	No	2.5
	B. L.	18	Yes	2.3	18	No	0.5
	S. W.	38	Yes	1.6	38	No	1.6
	S. L.	26	Yes	1.5	26	No	0.0
3	B. A.	50	Yes	4.0	50	Yes	3.0

Group 1 (marked reactors). In this series 27 per cent of all patients fell in the first group. Two minutes after the sublingual administration of 1/100 gr. of nitroglycerin, these patients were able to perform approximately 100 per cent or more work than had been possible without medication. When given other drugs, they showed a definite increase in exercise tolerance — usually 50 to 100 per cent — and practically complete disappearance of attacks in daily life. The electrocardiogram before treatment and immediately following exercise sufficient to produce pain showed an average depression of the RS-T segment of 2.03 mm., with a range of 1.0 to 2.7 mm. Following the administration of nitroglycerin or other effective vasodilating measures, the average of the RS-T deviations after the same amount of work was 0.2 mm., with a range of 0.0 to 0.5 mm.

Group 2 (moderate reactors). Thirty-three per cent of all patients comprised the second group. They could do approximately 50 per cent more work after receiving nitroglycerin than before. When given other effective medication, most of them showed a moderate increase in exercise tolerance (25 to 50 per cent) and a definite decrease but not complete disappearance of attacks in daily life. The average control deviation of the RS-T segment during pain was 2.43 mm., with a range of 1.5 to 3.5 mm., and after the same amount of work following nitroglycerin was 1.1 mm., with a range of 0.0 to 2.5 mm.

Group 3 (nonreactors). The remaining 40 per cent of patients showed no response to nitroglycerin and little response to most other methods of treatment. They showed the same electrocardiographic changes during exercise whether therapy had been given or omitted.

Group 3 contained a high percentage of women and a low percentage of thin persons and of patients whose illness began before the age of fifty. Hypertension was somewhat commoner in Group 3 than in Group 1, and there was a high percentage of patients with low exercise-tolerance tests. Striking exceptions were frequent, however, and in any given case no characteristics other than the response to therapy served to differentiate the groups. In particular, the frequency and severity of attacks and the frequency of cardiac hypertrophy or abnormalities of the electrocardiogram at rest were approximately the same in all three groups.

There was a striking difference in the mortality of the groups (Fig. 5). During the period of observation, death occurred in 15 per cent of the patients in Group 1, 28 per cent in Group 2 and 43 per cent in Group 3. Conversely, after ten years of illness, 30 per cent of the patients in Group 1 were still living as compared with 16 per cent in Group 2 and 3 per cent in Group 3. Viewed in the light of the pathological studies of Schlesinger, Blumgart and their associates,[16-18] this suggests that the patients in Group 3 represent those in whom the collateral circulation has compensated to the maximum extent. The coronary circulation

of such patients has little reserve, so that neither an increase in blood flow due to the use of vasodilators nor the development of additional anastomotic channels following additional coronary occlusion is possible. Patients such as those in Group 1, on the other hand, have developed a well-functioning system of anastomotic channels with considerable reserve, so that an increase in blood flow occurs with vasodilating drugs and additional collaterals develop following coronary occlusion.

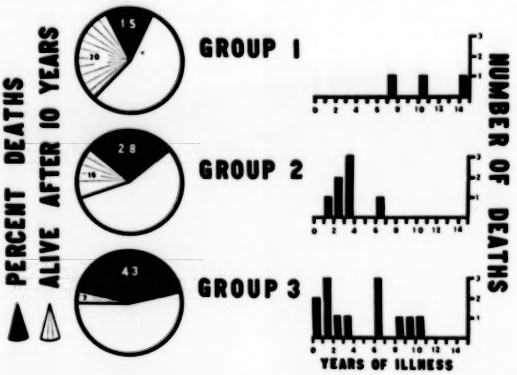

FIGURE 5. *Mortality in Patients with Angina Pectoris.*

During the course of observation, several patients showed a change in ability to respond to therapy. Five patients who originally responded strikingly (Group 1) later responded to a lesser degree (Group 2). A sixth became completely unresponsive to medication for several months (Group 3) and died. Similarly, 2 patients originally in Group 2 suddenly failed to respond (Group 3), and 1 died within a few months after this change. On the other hand, 4 patients originally in Group 3 improved during the period of observation; 2 were ultimately classified in Group 1 and the other 2 in Group 2. In at least 2 of these patients, the improvement occurred after recovery from an episode of myocardial infarction.

Comparative Value of Therapeutic Measures

The comparative value of sixty-eight different therapeutic agents can be separated into three groups — those of marked value, those of moderate value and those of no value — on the basis of clinical effectiveness, low toxicity and low cost (Table 2).

Clinical effectiveness. When a therapeutic agent is given in adequate doses, a definite increase in the standardized exercise tolerance and a corresponding decrease in the frequency of attacks in daily life usually occur, especially in Group 1 patients. This clinical improvement is usually accompanied by a decrease in the electrocardiographic changes following exercise.

Low toxicity. This includes not only freedom from untoward reactions but also ease and practicability of administration in clinical practice.

Low cost. The importance of cost to the patient lies in the fact that angina pectoris and its underlying coronary arteriosclerosis are chronic conditions and that treatment must be continued over a long period, usually for life. To be of practical value, therefore, therapy must be sufficiently inexpensive so that the patient will be able to continue treatment for as long as necessary. The marked difference in cost of various commercial preparations without regard to their clinical effectiveness has been illustrated.[8]

The therapeutic agents of *marked value* were of three types as measured by results. The majority of agents resulted in an increase in exercise tolerance of 30 to 100 per cent or more in at least half the patients in Group 1. A few agents — the sedatives, atropine and potassium iodide in large doses — were not of such striking value, but were of appreciable benefit to some patients in Group 3 for whom few other satisfactory agents were available. The surgical procedures — total thyroidectomy and alcohol injection — were included because although costly, difficult to perform and not infrequently accompanied by untoward effects,

TABLE 2. *Comparative Value of Methods of Treatment.*

TYPE OF THERAPY	DEGREE OF VALUE		
	MARKED	MODERATE	NONE
Nitrites	Nitroglycerin, 1/100 gr. Nitroglycerin, 1/500 gr. Octyl nitrite Amyl nitrite	Erythrol tetranitrate, ¼ gr., 4 times daily Mannitol hexanitrate, 1 gr., 4 times daily	Sodium nitrite, 1 gr., 4 times daily
Purines	Theobromine and sodium acetate, uncoated, 7½ gr., 4 times daily Theophylline and sodium acetate, uncoated, 3 gr., 4 times daily Theophylline and calcium salicylate (Phyllicin), 8 gr., 4 times daily Theobromine sodium acetate, enteric-coated, 7½ gr., 4 times daily Aminophylline, 3 gr., 4 times daily Theophylline methyl glucamine (Glucophyllin), 4 7/10 gr., 4 times daily	Theophylline, 4 gr., 4 times daily Theobromine, 5 gr., 4 times daily Theobromine and sodium salicylate (Diuretin), 7½ gr., 4 times daily Theobromine and calcium salicylate (Theocalcin), 15 gr., 4 times daily Theophylline diethanolamine (Dephyllin), 1 cc., 4 times daily Theophylline monoethanolamine (Theamin), 3 gr., 4 times daily	Caffeine citrate, 2 gr., 4 times daily Theobromine and calcium-gluconate (Calpurate), 15 gr., 4 times daily
Sedatives	Phenobarbital, ½ gr., 4 times daily Codeine sulfate, ½ gr., 4 times daily Cobra venom, intramuscularly	Theamin with amytal, 3¼ gr., 4 times daily Theominal, 5½ gr., 4 times daily Dilaudid, 1/20 gr., 4 times daily Bed-rest for 6 weeks	Papaverin, ½ gr., intravenously
Cinchona derivatives	Quinidine sulfate, 5 gr., 4 times daily Quinophylline (quinidine sulfate, 5 gr., and aminophylline, 3 gr.), 4 times daily	Quinine sulfate, 5 gr., 4 times daily	
Procedures or drugs acting on the autonomic nervous system	Pressure on the carotid sinus Atropine sulfate, 1/120 gr., 4 times daily	Physostigmine salicylate, 1/40 gr., 4 times daily Amphetamine (Benzedrine) sulfate, 1/12 gr., 4 times daily	X-radiation of adrenal glands X-radiation of thoracic sympathetic nerves Novatropine, 1/12 gr., 4 times daily Syntropan, 1½ gr., 4 times daily
Iodides and intravenous saline solution	Potassium iodide, 1 gm. enteric-coated tablets, 3 or 4 times daily	Normal saline solution, 500 cc. intravenously, daily Sodium chloride, 5% solution, 200 cc. intravenously, daily Sodium iodide, 5% solution, 200 cc. intravenously, daily	Potassium iodide, saturated solution, 15 drops, 3 times daily Lugol's solution, 15 drops, 3 times daily
Surgical	Total thyroidectomy Paravertebral injection of alcohol		Denervation of thyroid gland
Miscellaneous	Heat	Inhalation of oxygen during exercise Whiskey, 1 oz. before work Metrazol, 3 gr., 4 times daily Inhalation of trichlorethylene	Lactose Sodium bicarbonate, 5 gr., 4 times daily Calcium salicylate, 5 gr., 4 times daily Ethylene diamine hydrochloride, 1 gr., 4 times daily Coramine, 1 teaspoonful, 4 times daily Myorgal, 2 tablets, 4 times daily Depropanex, 2 cc., daily Dinitrophenol, 25 mg., 4 times daily Cigarette smoking Estrogenic substances, 10,000 I. U., daily Testosterone, 25 mg., daily Thiamine, 10 mg., 4 times daily Niacin, 50 mg., 4 times daily Kerr abdominal belt Digitalis Theophyllinated genin of squills[27]

they were nevertheless of striking value in a few patients not helped by other and simpler means.

The therapeutic agents of *moderate value* were those the administration of which was followed by some improvement but not of sufficient degree or frequency to recommend them for routine use, — especially since more valuable methods of therapy were available, — and those, such as oxygen therapy, that were clinically effective but were impractical for clinical use.

The therapeutic agents of *no value* resulted in no appreciable increase in standardized exercise tolerance. Any clinical improvement that followed their use could be ascribed to psychologic influence.

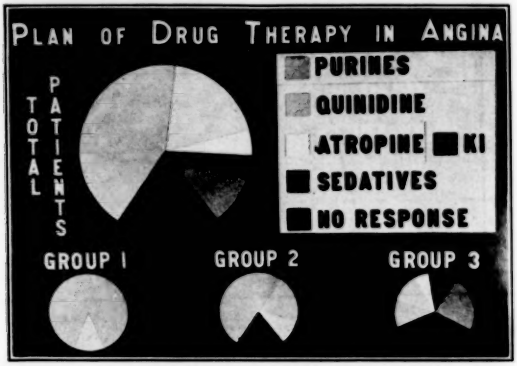

FIGURE 6.

ROUTINE TREATMENT

Treatment should be individualized. Careful questioning and prolonged observation may reveal specific precipitating factors — such as walking uphill or after meals, going out into the cold or emotional disturbances — that can be guarded against or eliminated. A change in habits, the use of sedatives or the prophylactic use of nitroglycerin at appropriate times is frequently of value in such cases. In a few cases (less than 1 per cent) hyperthyroidism, anemia, polycythemia or arrhythmias responsible for attacks may be discovered and corrected.

Medication is usually necessary. The purines are most likely to be of value (Fig. 6). Theobromine and sodium acetate, enteric-coated (7½ gr., four times daily), is the drug of choice. Theophylline and sodium acetate (3 gr.) and theophylline and calcium salicylate (8 gr.) are equally helpful but more costly. Aminophylline (3 gr.) is somewhat less valuable and is also more expensive. In using the enteric-coated preparations, it must be understood that several hours will elapse before they become effective (Fig. 7). It is important, therefore, to administer medication before the patient retires, for it is this dose that is effective on the following morning. In many cases it is advisable to give in addition a single dose of nonenteric-coated medication on the patient's arising. The purines were of benefit in 43 per cent of all patients (88 per cent in Group 1, 50 per cent in Group 2 and 12 per cent in Group 3).

In addition, especially during the first few weeks of therapy or if the symptoms are severe, it may be advisable to give 1/400 gr. of nitroglycerin under the tongue every hour when the patient is awake. Sedatives may be given as an adjunct. Although the latter may not increase the exercise tolerance to a striking degree, they help to stabilize the patient emotionally and make the pain easier to bear.

If this regime is of value, it will be evidenced within a week by the complete or almost complete disappearance of attacks in daily life. Any improvement short of this is probably not due to the medication used.

If no satisfactory response is obtained, it is advisable to substitute quinidine sulfate (5 gr. three or four times daily) as the drug next most likely to bestow benefit. Quinidine is about as effective as the purines, and the toxicity in patients with angina pectoris and normal cardiac rhythm is low. Sixty-one per cent of all patients were benefited by the purines or quinidine (all those in Group 1, 50 per cent in Group 2 and 24 per cent in Group 3).

The treatment of the remaining two fifths (39 per cent) of patients, especially those in Group 3, is a difficult problem, and future research should be directed toward the care of this group. Atropine sulfate (1/120 gr., four times a day) was of some value in approximately 10 per cent of such patients in Group 2 and 6 per cent in Group 3. Potassium iodide in comparatively large doses (1.0 gr. in an enteric-coated tablet, three or four times daily)[19] was of value in an additional 12 per cent in Group 3. The sedatives, especially codeine sulfate, helped another 20 per cent in Group 3. There remain about 20 per cent of all patients (two thirds of whom were in Group 3) who responded to none of these medications.

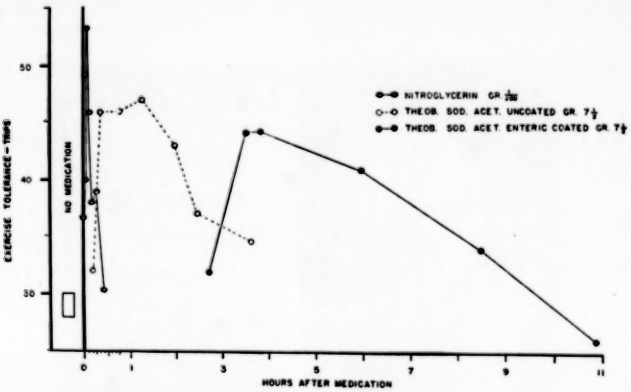

FIGURE 7. *Comparative Effect of Nitroglycerin and Theobromine Sodium Acetate, Both Uncoated and Enteric-Coated, in Patient S. W. (Group 2).*

Treatment of Severe Angina Pectoris

In many cases, especially in patients with severe angina pectoris who fail to respond to this regime, it is advisable to use a combination of therapeutic agents. While admittedly a "shotgun" method, the results obtained in such patients and the absence of other simple effective therapeutic measures justify its use.

Such patients should have a period of complete bed rest combined with adequate sedatives and small hourly doses of nitroglycerin. In some cases it is advisable to give in addition adequate doses of an active purine and, if necessary, quinidine sulfate. This regime usually results in the complete disappearance of pain within a week, unless there has been a recent coronary occlusion or unless a strong emotional element is present.

If the symptoms reappear when the patient returns to normal activity, cobra venom is worthy of a trial.[14, 20] This drug diminishes attacks without affecting the underlying cardiac mechanism responsible for the pain. It must be given by injection, daily for at least a week and two or three times weekly thereafter.[14] Despite these drawbacks, cobra venom, in certain cases, obviates the necessity for surgery.

Only if these measures fail to give relief should surgery be considered. Few patients, however, come to surgery (Fig. 8). At the Beth Israel Hospital, in 46 per cent of the patients with angina pectoris the disease was so mild even without therapy that surgery was unnecessary. In an additional 24 per cent, the response to medicinal therapy (exclusive of cobra venom) made surgery unnecessary. Of the remaining 30 per cent, approximately half were unsuitable surgical risks, and half the remainder refused operation when the risk and the likelihood of benefit were explained. As a result, surgery was performed in approximately 7 per cent of patients with angina pectoris.

In our experience, total thyroidectomy[21, 22] has given more striking results than has any other form of therapy (Fig. 9). It is the surgical procedure of choice in patients with normal basal metabolic rates, prolonged but nonprogressive symptoms and a fair life expectancy who are adequate surgical risks. Suitable cases are admittedly few, but thyroidectomy may be a valuable means of alleviating symptoms and restoring physical ac-

tivity in those few to whom there is little else to offer.

Some form of surgery of the sympathetic nervous system may be employed in patients not suitable for total thyroidectomy. Alcohol injection is at present considered to be the method of choice, but it rarely results in any increase in exercise tolerance and may be followed by a neuritis.[23-26] The comparative freedom from pain that occurs in some patients, however, justifies the use of this method in the few selected patients who may require such relief.

Experience has shown that the above plan goes a long way toward prevention of attacks of angina pectoris. It has enabled many patients to increase their physical activity and in some cases to return to gainful occupation. Information concerning prolongation of life is difficult to obtain, but it is logical to reason that freedom from attacks indicates comparative freedom from the physiologic mechanism responsible for some of the complications.

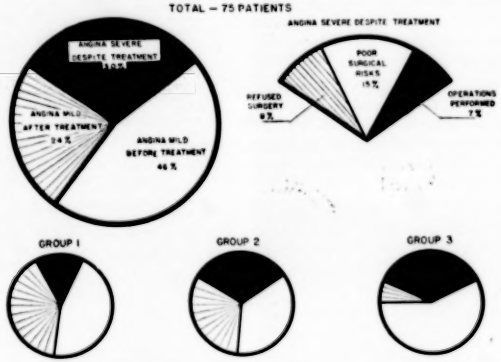

FIGURE 8. *The Frequency of Surgical Treatment in Angina Pectoris.*

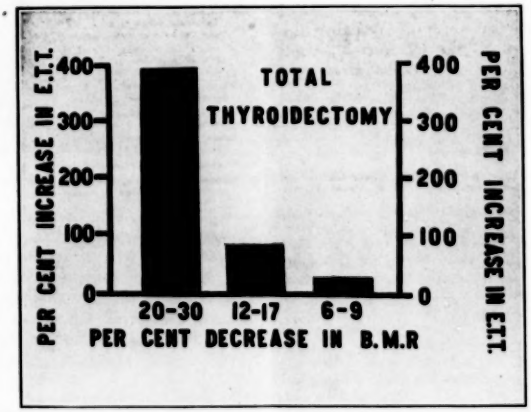

FIGURE 9.

SUMMARY

An objective evaluation of the efficacy of treat-

ment of angina pectoris carried out over a ten-year period shows that 27 per cent of patients respond strikingly to practically all available forms of therapy, 33 per cent respond to a moderate degree, and 40 per cent usually fail to respond appreciably. This variation in therapeutic response should be taken into account in any study of the efficacy of treatment of angina pectoris.

The clinical evaluation of the efficacy of therapy is extremely difficult and unreliable. Nothing short of complete or almost complete disappearance of attacks can be considered as a favorable response, and it must be remembered that such periods may be spontaneous and not related to treatment.

Of the sixty-eight methods of therapy evaluated, twenty were found to be of considerable value, twenty-two were of slight value, and twenty-six were of psychologic value only.

In prescribing medicinal therapy, the drugs of choice are nitroglycerin (1/400 gr. every hour), theobromine and sodium acetate (7½ gr., four times daily), quinidine sulfate (3 to 5 gr., four times daily), atropine sulfate (1/150 gr., four times daily), enteric-coated potassium iodide (1.0 gm., four times daily), cobra venom (given intramuscularly) and the sedatives. The plan of treatment outlined was of value in approximately 80 per cent of all patients.

Few patients require surgery. Total thyroidectomy is of considerable value for selected patients. The paravertebral injection of alcohol gives symptomatic relief to others.

45 Bay State Road

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CLINICAL NOTE

LARYNGOPYOCELE

Report of a Case

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BOSTON

A LARYNGOCELE or aerocele is supposed to be a congenital sac due to a prolongation of the ventricle of Morgagni. It is normal in certain groups of monkeys and is then bilateral. It is sometimes referred to as a "monkey pouch." The literature contains reports of about 80 cases in human beings, by far the greatest proportion being found at autopsy or in dissecting rooms. The presence of pus in the laryngocele is rare, and in the case reported below may have taken place at the time of the patient's extremely "sore throat" a year and a half previous to examination.

Figure 1. *X-Ray Films Taken in the Lateral and Anteroposterior Positions.*

Case Report

A 45-year-old woman, referred by Dr. W. W. Marston of Newton, had complained of hoarseness intermittently for 1½ years. She had received a satisfactory tonsillectomy 25 years previously. She had had a very sore throat 1½ years previously.

Examination of the larynx showed that the left cord was normal in color and motion. The epiglottis and tracheal rings seemed normal. The right cord was red and indistinct and was partly obscured by a red and protruding false cord. There was some limitation of motion on the right side, as well as marked fullness on the outside of the neck just to the right of the larynx. The roentgenologist (Dr. A. S. MacMillan) reported an aerocele of the right ventricle (Fig. 1).

At operation, an oval sac measuring 2 by 3 cm. was located at the right of the thyroid cartilage, extending up to the cornu of the hyoid bone and reaching posteriorly and laterally to the region of the superior laryngeal nerve. Its wall was thin and slightly adherent at the fundus. The other end of the sac took the form of a neck that penetrated the thyrohyoid membrane and curved over the superior border of the thyroid cartilage, passing down its inner surface and under the right false cord to its origin in the ventricle of Morgagni. The sac was removed after suturing and severing the neck. It was filled with a fluid pus, thus making it a pyocele and not an aerocele. A stained smear of the pus showed gram-positive bacilli, and a culture was negative for beta-hemolytic streptococci. The pathologist's report was as follows: "The specimen consists of a small oval cystic structure opened at one end and measuring 3.5 by 2.0 by 1.0 cm. Its outer surface is roughened from resection. The wall is fibrous and less than 1 mm. in thickness. The lumen is empty, and the lining is smooth and pinkish gray. Microscopically, the cyst-like cavity is lined by ciliated columnar epithelium, supported by stroma that is rich in lymphocytes and at one point shows a nest of mucous glands. Diagnosis: laryngocele?"

The patient made an uninterrupted convalescence. After 2 weeks the wound was healed, the hoarseness had disappeared, and the appearance and motion of the larynx had become normal.

Those seeking further information on this rare condition are referred to an excellent article by

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Freedman,[1] published in 1938. He outlines the history of the discovery of the laryngeal ventricles, sometimes called the ventricles of Morgagni because of the latter's detailed description given in 1741. Freedman refers to the fine dissections made of this space by Hilton[2] in 1837 and to the discovery of the sacculus laryngis, which contains many mucous glands; he ventures the theory that these glands furnish the fluid to lubricate the vocal cords. He then elaborates on the physiology of this function of the sacculus, and on the consequences of its failure. The sacculus or its extension, he says, represents the air sac of the anthropoid apes. Freedman expounds the theory that apes and other climbing mammals are at times forced to cease breathing temporarily, and that these air sacs are filled with oxygen on inspiration but with carbon dioxide during expiration, and therefore act as mixing chambers. He reports a case of pyocele in a fifty-four-year-old man and describes his operative technic. He also cites a case of prolapse of the sacculus and a laryngocele in a nine-week-old boy. His article ends with references to ten other articles.

Jackson and Jackson,[3] in their textbook published in 1937, state that laryngocele is a very rare disease and that they have seen only 2 cases. In both these cases the sac protruded into the lumen of the larynx and not into the neck, and contained air and not pus as in the case here reported.

Summary

A case of laryngopyocele is reported, and the pertinent literature is discussed.

101 Beacon Street

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MEDICAL PROGRESS

PANCREATIC INSUFFICIENCY AND THE CELIAC SYNDROME (Concluded)

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BOSTON

Pancreatic-Enzyme Analysis

THE frequent familial history, the apparently congenital nature of the process, the early onset of symptoms and the presence sooner or later of pulmonary infection assist in the clinical differentiation of pancreatic insufficiency from idiopathic celiac disease. Measurement of the activity of pancreatic enzymes in the duodenal content, however, appears to be the most valuable single laboratory aid in making this differentiation and in establishing the diagnosis in the absence of symptoms of the celiac syndrome. Two recent extensive studies of pancreatic-enzyme activity in infants and children, with particular reference to the celiac syndrome, have been made. Andersen[26] included data on such activity in the duodenal content of 15 patients who had a clinical history consistent with the diagnosis of pancreatic fibrosis, in a report of enzyme studies on 98 infants and children including some with chronic diarrhea, others with extreme marasmus and some with a classic picture of true celiac disease. Farber, Maddock and Shwachman[25] presented data on the pancreatic-enzyme activity of 150 infants and children including normal patients with chronic nutritional failure, 11 with true celiac disease and 22 with pancreatic fibrosis. The results of these studies, in agreement with all similar observations, such as those by Siwe,[27] Benoit,[28] Tiling[29] and others[30] who have studied pancreatic enzyme activity in the celiac syndrome in small numbers of patients, demonstrated that markedly diminished or absent activity of pancreatic enzymes in the duodenal content, particularly that of trypsin and lipase, characterizes all cases of pancreatic fibrosis, in contrast to the essentially normal values found in patients with true celiac disease and other types of chronic failure of nutrition. An important pancreatic lesion was found at autopsy in every patient in whom pancreatic achylia had been demonstrated during life. Farber, Maddock and Shwachman state that patients with sprue, idiopathic steatorrhea or that form of the celiac syndrome associated with malrotation of the bowel have normal pancreatic enzyme activity and do not differ in this respect from patients with true celiac disease. The duodenal content in patients with pancreatic fibrosis is frequently so striking in its scantiness and viscidi-

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual.* Volume III. 678 pp. Springfield, Illinois: Charles C Thomas, 1942. $5.00).

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ty that diagnosis may be made with considerable accuracy on gross inspection alone. All patients with chronic nutritional failure may be divided provisionally into two large groups on the basis of pancreatic enzyme analysis: those with normal activity and those with markedly reduced or absent activity. From this temporary classification further subdivision may be carried out in the group with normal enzyme activity. The generalization has been made that the diagnosis of true celiac disease, idiopathic steatorrhea, nontropical sprue, pancreatic fibrosis or other similar conditions should not be considered as established until the pancreatic-enzyme activity in the duodenal drainage has been measured.

Andersen[26] has recognized two groups of patients who may be separated from those with celiac disease and with pancreatic fibrosis on the basis of enzyme analysis. She found some patients with what she called "near-celiac" disease who showed intolerance to starch in the diet, a low level of amylase in the duodenal juice, and starch in the stools but no excessive stool fat. Such patients have a relatively mild, though prolonged, clinical course. In the second group she placed those with idiopathic steatorrhea, intolerance to fat, a high concentration of stool fat, normal amounts of pancreatic enzymes and a severe and protracted clinical course. She suggests that in these patients the difficulty lies in the absorption rather than in the digestion of fat. In 3 patients with severe marasmus she found depression of activity of trypsin, amylase and lipase, with a return to normal after clinical improvement. Farber, Maddock and Shwachman[25] encountered patients with failure of nutrition in whom selective lipase deficiency was demonstrable in the presence of normal amounts of trypsin and amylase. They reported also the demonstration of absence of tryptic activity in an infant with meconium ileus.

Andersen[26] has suggested that the assay of trypsin alone is a reliable means of diagnosis of pancreatic deficiency. In general, she states that few errors in the diagnosis of pancreatic fibrosis will be made if amylase and lipase are not measured. Rare exceptions may be encountered, such as a case of selective trypsin deficiency in a boy with chronic nutritional failure that did not resemble the celiac syndrome; in the duodenal content normal amylolytic and lipolytic activity was demonstrated.[25] Particularly during the first few months of life, the assay of amylase yields little information of value, since this enzyme is present in such low concentration in normal infants.[31] In many older infants and young children with chronic diarrhea amylolytic activity in the duodenal content may be reduced.[26]

It appears probable that further anomalies of pancreatic exocrine function will be discovered when studies of pancreatic activity are carried out on large series of infants and children. In patients with pancreatic fibrosis Maddock, Farber and Shwachman[32] found that stimulation of the pancreas by secretion had little effect on the duodenal content and was not essential for the correct interpretation of the enzyme activity in the pancreatic juice. Stimulation by secretion, however, causes a moderate increase in amylolytic activity in patients with true celiac disease and a marked rise in those with chronic nutritional disturbances of the nonceliac type.[32]

Pancreatic achylia appears to be a permanent finding unaffected by pancreatic substitution therapy or any other form of treatment, since six determinations of enzyme activity in the duodenal content of a patient made between the ages of five and twenty-five months showed no appreciable change in the level of enzyme activity, although the patient's general condition appeared to improve.[25]

Detailed descriptions of methods of pancreatic-enzyme analysis for use on infants and children have been given.[26, 33, 34] It appears clear that this field of investigation, opened by the pioneer work of Hess[35] on infants in 1912, will have much value. The use of Mecholyl and secretin in studies of pancreatic function should yield data of great interest.[36]

Metabolic Studies

Shohl, May and Shwachman[37] found the weight of the feces of patients with pancreatic fibrosis to be greater than that in any other condition in childhood. In a series of metabolic studies designed to furnish data concerning altered nitrogen metabolism in pancreatic fibrosis under controlled conditions, when native protein was removed from the diet, there was no difference in the weight of the feces. When both protein and fat were omitted, however, and nutriment was given parenterally, the residue of the feces was small. Pancreatic substitution therapy was followed by reduction in the weight of the feces, but not to the normal level. Those writers concluded that the amounts of nitrogen in the feces of patients with pancreatic fibrosis may exceed that in the urine and reach three or four times that in the feces of normal infants. Excessive nitrogen in the feces is the cause of a negative nitrogen balance and is partly responsible for the loss of weight and the deterioration of patients with this disease. With respect to high fat in the stools, excessive excretion of nitrogen in the feces and marked increase in the weight of the stools, children with pancreatic

fibrosis behave as do dogs in which the pancreatic juices have been excluded from the intestines. Shohl et al. were able to reduce the amount of fecal excretion and nitrogen excretion in the feces to normal limits when a fat-free ration, consisting of casein hydrolysate and glucose, was administered.

It may be of interest to mention the similar results of metabolic studies in 4 adults with pancreatic achylia reported by Beazell, Schmidt and Ivy.[38] Although the etiologic factors were unknown, the diagnosis was made on the basis of an absence of pancreatic enzymes in the duodenal drainage, an increase in the quantity of nitrogen and fat in the feces and a reduction in the wastage of both nitrogen and fat with substitution therapy. The patients were placed on a standard balanced diet supplying 64 gm. of protein and 112 gm. of fat daily for a period of six days. Beginning with breakfast on the fourth day, the patients were given with each meal 8 gm. of pancreatin in the form of enteric-coated tablets. A total of 24 gm. was given daily, one half immediately before and one half immediately after the meal. The 24 gm. corresponds to approximately 240 cc. of pancreatic juice, which represents only 15 per cent of the quantity normally estimated to be secreted by adults within twenty-four hours. After one month on this dose, the daily dose was progressively reduced until only 2 or 3 gm. was given with each meal. Response was noted by observing the subjective reaction, the character of the stools, the reduction in the frequency of stools, the gain in weight and the increased strength. These authors state that they have never seen pancreatic achylia, either clinically or in an experimental animal, that failed to respond to adequate enzyme therapy. Conversely, in the absence of demonstrable pancreatic insufficiency enzyme therapy never effected reduction in the nitrogen or fat of the stool.

Although steatorrhea has been stressed as one of the most characteristic findings in both pancreatic fibrosis and celiac disease, to the extent of including the word in the name of the disease,[18] wide variations in the amount and kind of fat in the stool may be encountered. It should be recalled that the fat content of stool specimens of normal infants and children varies from 10 to 80 per cent of the dried feces.[39] Andersen[40] found that it increased to 30 to 80 per cent of the dry weight when the patient was given a whole-milk formula or an average mixed diet. Only 7 of the 35 patients with pancreatic fibrosis proved at autopsy studied by Blackfan and May[15] had stools that were described as fatty. Examination of the stools of patients with pancreatic fibrosis for the ratio of neutral fat to hydrolyzed fat[41] has not served to differentiate this disease from celiac disease, since fat may normally be split by intestinal lipase in the absence of pancreatic lipase.[42]

In the entire group of celiac diseases, absorption of fat is disturbed, although the mechanism may differ from case to case. Measurement of the absorption of vitamin A from the intestines was proposed by Breese and McCoord[43] as a test to aid in the diagnosis of celiac disease. The studies of May and McCreary[44] show that a low rise in the vitamin A absorption test is found in both celiac disease and pancreatic fibrosis. Differences in the degree of decreased absorption of vitamin A are detectable, but are not great enough to be of aid in differentiating these two conditions in a given patient. May and McCreary found no improvement in true celiac disease in the absorption of vitamin A when the vitamin was introduced intraduodenally and active intestinal peristalsis was maintained with Mecholyl.

An observation of considerable importance concerning the increased absorption of vitamin A in pancreatic fibrosis when the motility of the bowel is increased has been described by Flax, Barnes and Reichert.[30] Proceeding on the assumption that the inefficient absorption of vitamin A as well as of glucose is probably associated with the lack of tone and abnormal motility of the intestinal tract, they administered Prostigmine parenterally to a patient with pancreatic fibrosis and observed an almost immediate rise in the blood level of vitamin A. They chose this drug because of its success in restoring muscle tone in postoperative ileus.[45] After a period of five months, during which Prostigmine Bromide was given in amounts of 7.5 mg. three times a day, the absorption of vitamin A showed a normal curve. A rise in the total blood-cholesterol level was also observed, which suggested an increased lipid absorption. Of considerable interest was a diminution in the cough with decreased evidence of lung infection on roentgen-ray examination, a change that these writers attribute to better absorption of vitamin A brought about by increased motility of the bowel.

A low blood-sugar curve in the glucose-tolerance test is found in true celiac disease.[2] Andersen[40] has pointed out that the glucose-tolerance curve in pancreatic fibrosis, although usually flat, may show an initial sharp rise and a rapid fall, as in the hunger curves described by Harris. Normal values are encountered. The low rise of the curve in celiac disease was at first interpreted as a change secondary to diminished gastrointestinal motility. May, McCreary and Blackfan[6] found, however, that when a solution of 3 per cent glucose containing as much glucose as was given ordinarily in a 10 per cent concentration was introduced intraduode-

nally in patients with celiac disease, the level of glucose in the blood did not rise more than 40 mg. per 100 cc. even if active intestinal motions were maintained by means of Mecholyl. When patients recovered from celiac disease, however, a normal rise in the blood sugar occurred following the simple intraduodenal administration of glucose in a 3 per cent concentration. Although intestinal motility plays an important role in intestinal absorption, there must be in addition in celiac disease an impairment of absorption of glucose by the intestinal mucosa. No adequate explanation has been offered for the poor absorption of glucose when it does occur in patients with pancreatic fibrosis.

Roentgenologic Studies

In both pancreatic fibrosis and celiac disease clumping of the barium meal in roentgenograms of the small bowel similar to that observed by Snell and Camp[46] in adults with steatorrhea and in vitamin B deficiency states[47] was found with regularity by Blackfan and Vogt,[48] and was explained by May and McCreary[44] by the impairment of peristalsis and tone and by segmentation of the bowel. Alternate segments showing spasm and dilatation with loss of the normal pattern of the valvulae conniventes characterize the roentgenologic picture. This abnormality in the motility of the bowel may be temporarily corrected by Mecholyl.[44]

Attwood and Sargent[49] have described the roentgen-ray appearance of the pulmonary lesions that are so consistently a part of the disease at any time after the first few weeks to months of age. They reported an increase in the density of hilar shadows, with loss of definition and prolongation outward into a surrounding mottling that gradually diminishes toward the periphery of the lung. The changes are bilateral and are symmetrically distributed about the roots of the lungs and the adjacent parenchyma. The changes in the upper lung fields are quite as marked as those at the bases. These writers warn against the danger of making an erroneous diagnosis of tuberculosis in patients in whom the illness is prolonged, because of the marked chronicity of the pulmonary lesions. Neuhauser[50] has divided the lung changes into two stages corresponding to the pathologic picture. The first is characterized mainly by emphysema and atelectasis dependent on the partial or complete obstruction of bronchi and bronchioles by the tenacious mucus or mucopurulent exudate. Atelectasis is at times difficult to recognize, since the small shadows of increased density resemble areas of pneumonic consolidation. Obstructive emphysema is identified with less difficulty by the decreased density, the bulging spaces and the widening of the intercostal spaces. In the later or second stage, the roentgenologic changes become more marked, with patchy areas of peribronchial infiltration and areas of bronchiectasis. The process is marked toward the hilum, and the bronchovascular and interstitial markings radiating from each hilum are increased. The end stage is that of pneumonic infiltration, bronchiectasis and bronchiectatic abscesses, with varying degrees of atelectasis and obstructive emphysema. It should be stressed that these x-ray manifestations of pulmonary disease are by no means limited to patients with pancreatic achylia. They occur so frequently, however, in patients with this disorder that studies designed to confirm or exclude this diagnosis, such as analysis of pancreatic-enzyme activity, should be carried out whenever such changes are encountered.

Treatment

The outstanding disturbances produced in this disease, either by the pancreatic insufficiency or by the alterations elsewhere in the body, include absent or greatly reduced pancreatic-enzyme activity, particularly of trypsin and lipase; malabsorption of vitamin A; loss of nitrogen in stools; and upper respiratory obstruction and infection leading to bronchiectasis and bronchopneumonia. Treatment may be directed logically along these four channels. Pancreatic substitution therapy is indicated by the pathologic picture and the demonstration of pancreatic hypochylia or achylia. It has been found of value in infants and children and in adults with pancreatic insufficiency.[37, 38, 40] The greatly diminished absorption of vitamin A that has been demonstrated by the vitamin A absorption test,[43, 44] as well as by the occasional finding of histologic evidence of vitamin A deficiency,[14] may be corrected either by enteral or parenteral administration of vitamin A.[30, 40] Intramuscular injection of preparations of vitamin A in large doses has been recommended.[30] The marked loss of nitrogen in the stools may be corrected in part by pancreatic substitution therapy and in part by a direct replacement of lost nitrogen in the form of casein hydrolysate.[37] Infection in the lungs is an almost invariable accompaniment of the disturbance in nutrition. Since the most frequently found organism is *Staph. aureus*, and since it is one of apparently low virulence, chemotherapy is indicated, although difficulty is encountered in finding a completely effective form of specific therapy.

Flax, Barnes and Reichert[30] have recommended the parenteral administration of Prostigmine to improve the muscle tone in the intestinal tract and so permit enhancement of nutrition in general

and absorption of vitamin A in particular. They summarize their therapeutic regimen as follows: a high-calorie, high-protein, moderately low-fat and low-starch diet; pancreatin granules, 1-5 gm. daily; vitamin A, 50,000 international units daily, in divided doses; adequate amounts of vitamins B, C and D; and Prostigmine Bromide, 3.75 to 7.50 mg. three times daily. Andersen[51] recommends a diet essentially similar to that used in celiac disease, with two important differences: hexose and sucrose, which can be utilized, are given instead of starch, and if pancreatin is administered a moderate amount of fat can be utilized. She used a diet high in protein, moderately low in fat and free from starch but not from sugar, and emphasizes the value of a caloric intake 30 to 50 per cent greater than that calculated for the given age to compensate for the loss of food in the stools. Although the parenteral injection of vitamin A concentrate or carotene was logical in theory, it was disappointing in practice. Much better results were obtained by the oral administration of large doses (15 drops) of percomorph or haliver oil three times a day.

At the Children's Hospital, Smith[52] emphasizes the importance of good hygienic surroundings, with special reference to prevention of upper respiratory infection, and recommends the immediate and intensive treatment of all infections with some chemotherapeutic agent. In some infants a small maintenance dosage is continued for longer periods. The disturbed nitrogen metabolism is cared for most satisfactorily by the use of casein hydrolysate preparations, as described by Shohl and his coworkers.[37] Pancreatic substitution therapy is given in the form of minute granules each of which is enteric coated (Panteric Capsules, Parke Davis). The granules are sprinkled on the food and are given in amounts of 2 to 5 gm. daily in divided doses. Special attention is paid to a high vitamin intake with especially large doses of vitamin A. Glucose is added to the diet to increase the caloric content. Intravenous and parenteral fluids are given according to indications in the given case.

Until recently all patients with proved pancreatic fibrosis have died, as has been clearly shown in recent studies.[53-58] Before pancreatic-enzyme studies were used, it was impossible to be certain of the diagnosis in patients said to have recovered from this disease. Recently a number of infants have been kept alive longer than was previously possible and some have improved markedly under a form of treatment similar to those discussed above.[51, 52] The great power of regeneration possessed by the exocrine portion of the pancreas[59] gives hope for resumption of pancreatic function if the cause of the obstruction can be removed. The form of treatment recognized for this removal, however, remains to be found.

In most cases the pulmonary lesions are responsible for death. Avoidance of infection is only one, albeit an extremely important, aspect of the problem. The markedly thickened mucus, responsible for the partial obstruction of the respiratory tract and the consequences thereof and for the pertussis-like cough, is one of the most important variable factors influencing the prognosis. It is representative of what may be present in other secretions in the body, if the disease is a systemic one, as pathological studies indicate.[16]

Conclusions

Adequate pancreatic substitution therapy, replacement of the large amounts of nitrogen lost in the stools and the administration of vitamin A and other therapeutic measures designed to correct the consequences of pancreatic achylia and the supposed error in fat absorption will do much to care for the pancreatic aspects of the problem. The disease is unfortunately much more than a lesion of the pancreas, and indeed, the great amount of attention paid to the pancreas in the recent literature, and even in this discussion, may serve to increase the neglect of the respiratory and other changes that emphasize the systemic nature of the process. Further studies are required to clarify and delimit the clinical disturbances associated with this disorder. Pathological studies[20] indicate that there exist combinations of organ involvement in this systemic disease the clinical counterparts of which have not yet been defined. The most frequently encountered combination is that of pancreatic and pulmonary disease, as emphasized above. In some cases the pancreas, lung and liver all show significant lesions, with biliary cirrhosis the most striking pathologic finding. Finally, involvement of the lungs and the liver, with no disease in the pancreas, and therefore absence from the clinical picture of those symptoms referable to pancreatic insufficiency, provides further evidence for the systemic nature of the underlying disease process, and places the lesion in the pancreas in its proper setting.

The studies that were undertaken to terminate the confusion of idiopathic celiac disease with pancreatic steatorrhea have satisfactorily accomplished their purpose. And they have done more. Several dissimilar clinical disorders — meconium ileus, chronic bronchopneumonia and pancreatic insufficiency and a celiac-like disease associated with chronic pulmonary disease — have all been found associated with the same obstructive pancreatic lesion, and valuable metabolic and thera-

peutic studies, suggested by the nature of this lesion, have been successfully accomplished. Finally, this apparently unrelated group of clinical disorders has been shown to possess logical interrelations by the demonstration that the pancreatic and pulmonary lesions are manifestations of a common disorder involving many secretion-forming structures in the body in a systemic disease. The definition of further clinical disturbances produced by this systemic disease and the clarification of the nature of the underlying process are tasks that remain to be accomplished. A satisfactory nomenclature, which has so far evaded the workers in this field, would do much, if not to hasten progress, at least to facilitate a discussion of this subject.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 29431

PRESENTATION OF CASE

A seven-and-a-half-week-old male infant was admitted to the hospital because of diarrhea.

The infant was delivered following eighteen hours of labor, but breathed and cried normally and weighed 8 pounds, 14 ounces. A formula containing Similac was used and the child seemed to tolerate it well. He continued, however, to pass meconium in small, frequent stools for the first six days, and he was given two doses of castor oil, following which he passed small yellow formed stools for one week. He left the maternity hospital on the tenth day, weighing 7 pounds, 14 ounces, on a formula consisting of 8 ounces of evaporated milk, 1 ounce of Karo and 16 ounces of water, with six feedings a day. He failed to gain weight and was admitted to a community hospital, where he remained for two and a half weeks. His stools at first were watery but later became formed and of normal color. He vomited considerably. The day following discharge, the stools became watery again, associated with vomiting but no fever. His physician tried Biolac without success. On evaporated milk and Karo, however, the stools became semi-soft, copious, excessively foul smelling and yellow, rapidly changing to gray. During the week before admission there were six to eight bowel movements a day. The baby's appetite was said to have always been good, but he was irritable. He had received 50 mg. of vitamin C daily, as well as capsules of vitamins A and D. There had been no hematemesis, melena, bloody stools or jaundice. No history of recent infection could be elicited.

A twenty-month-old sister had recently died of "pancreatic fibrosis" in the same local hospital. Another sister had died of peritonitis at one week of age in another local hospital.

Physical examination showed a thin, pale, undernourished, moderately dehydrated, underdeveloped, screaming infant, weighing 7 pounds, 4 ounces. The eyes, ears, nose and throat were normal. The lungs were clear. The heart was normal. The abdomen was moderately distended. There was moderately active peristalsis. The skin over the extremities and chest was loose. Examination was otherwise normal.

The temperature was 97°F.

The blood showed a red-cell count of 4,210,000, with 14.5 gm. of hemoglobin. The white-cell count was 17,400, with 37 per cent neutrophils, 53 per cent small lymphocytes, 9 per cent large lymphocytes and 1 per cent monocytes. The urine gave a + test for albumin, and the sediment contained 15 to 20 white cells and occasional red cells per high-power field. The stools were light gray, hard, formed, guaiac negative and positive for fat. A stool culture was negative for pathogenic bacteria. The blood protein was 4.2 gm. per 100 cc., the cholesterol 122 mg. per 100 cc., the chloride 101.7 milliequiv. per liter, and the sodium 130 milliequiv. per liter.

X-ray films of the chest were negative, and films of the skull showed a somewhat anteroposteriorly drawn-out skull, with relative overdevelopment of the posterior fossa. The sutures and fontanelles were open.

The baby was placed on a formula of evaporated milk 7 ounces, Karo 1 ounce and water 12 ounces. His appetite was good. During the first week the stools were yellow, soft to formed and only occasionally watery. They numbered two to four daily. There was a slight increase in weight. At the end of the first week, the formula was changed to evaporated milk 9 ounces, Karo 1 ounce and water 11 ounces, in six feedings. The stools became copious, gray and foul smelling, and the baby began to vomit. Duodenal-enzyme analysis showed absent trypsin. At that time a discharge summary received from the community hospital where he had been treated, stated that a diagnosis of idiopathic pancreatic fibrosis had been made and that he had been discharged on pancreatic extract, 2 capsules daily. The fasting carotenoid level was noted to have been 1.8 units per 100 cc., and the vitamin A level 7.5 units.

On the eighth hospital day, the baby was placed on pancreatic extract, 1 granule three times a day, 15 drops of Navitol, a teaspoonful of vitamin B complex and 25 mg. of cevitamic acid. He did not pick up, and an attempt was made to mix Nutramigen and pancreatin with whole boiled milk, supplementing these by vitamin K and liver extract intramuscularly twice weekly. The red count was 2,970,000, with 11 gm. of hemoglobin, and the white-cell count was 10,000. The stools were formed, green to yellow, almost fat free but guaiac positive. The total blood protein was 3.9 gm. per 100 cc. The weight was 7 pounds. He refused about half his feedings or vomited most of those he took. At the end of the second week he

*On leave of absence.

was placed on a formula consisting of 18 ounces of 2 per cent milk and 1 ounce of Karo supplemented by 5 gr. of pancreatin, which was steadily increased until he was getting 5 gm. of pancreatin. Vitamin D was furnished by ultraviolet irradiation. He was given repeated small transfusions of whole blood, which raised the red-cell count to 5,900,000, with 17 gm. of hemoglobin, on the eighteenth hospital day. He had two transfusions of plasma. The baby's condition seemed to improve considerably. The weight was 7 pounds, 8 ounces, on the twenty-fifth day, at which time he was having four small bowel movements daily.

On the thirtieth hospital day the temperature rose to 101°F. and the white-cell count to 19,000 and the baby was noted to have a weak cough. Physical examination and x-ray films of the chest were negative. He was, however, placed on sulfadiazine. The following day he developed vomiting and diarrhea, was taken off fluids by mouth and placed on intravenous and subcutaneous fluids. On the thirty-second hospital day the temperature rose to 103°F. The eardrums appeared inflamed but paracentesis yielded no exudate. Lumbar puncture was negative. Blood cultures gave no growth. He developed increasing respiratory distress, but the x-ray films of the chest remained negative. The respirations dropped to 8, and the heart became weak. The veins were collapsed, and the blood dark. Whole-blood transfusion and intranasal oxygen brought no improvement, and the baby died on the thirty-fourth hospital day.

Differential Diagnosis

Dr. Ralph A. Ross: The fact that this baby passed meconium stools for six days is significant, because ordinarily at the end of the third day meconium stools have ceased, and with an infant taking a reasonable formula, one expects to see beginning milk-curd stools. Apparently this was a matter of concern to the physicians in charge because the child was given two doses of castor oil.

The administration of castor oil in some circles has been used, I think, in an attempt to affect what is called meconium ileus, a rather rare instance of sticky meconium that cannot be passed on by the normal peristaltic movements of the bowel. In some hospitals the giving of castor oil has been made more or less routine on the third day, if there is any question about the stools. I believe, however, that castor oil is a drug that should never be used—perhaps I should say "hardly ever"—in the newborn period. If the expected effect of giving castor oil is to release the sticky meconium, it seems completely impossible that that can be accomplished by the administration of a violent irritant to the bowel. It is more likely that the meconium will completely obstruct the bowel and that the hyperactivity of the gastrointestinal tract will lead to a disastrous outcome.

The loss of weight of 1 pound is more than should occur in a normal child at the age of ten days.

The foul-smelling gray stools point to the presence of excess amounts of fat.

One can only question whether the sister who died at the age of one week suffered from meconium ileus and had a rupture of the intestine with peritonitis.

On admission the infant's weight was 1 pound, 10 ounces, lower than at birth. He was only moderately dehydrated and was screaming, and was therefore not in collapse or shock from dehydration. A moderately distended abdomen in an emaciated child is an abnormal finding and points to some severe difficulty.

"The temperature was 97°F." This low reading may have been due to exposure, but in an infant in such a debilitated state the low temperature may very well have been a sign of severe infection. The blood counts for a newborn infant were within normal limits. The white and red cells in the urine possibly point to some infection in the urinary tract.

The sodium was definitely low, which indicates loss of excessive amounts of sodium, probably through the gastrointestinal tract.

There is no indication that a gastrointestinal series was done. Is that correct?

Dr. Benjamin Castleman: Yes.

Dr. Ross: "Duodenal-enzyme analysis showed absent trypsin." That is a significant finding and almost pathognomonic. There is no note about presence of a lowered level of lipase in the duodenal enzyme. The level of amylase at this age is so low that it can barely be read.

The fasting carotenoid level was noted to have been 1.8 units and the vitamin A 7.5 units. These so-called "blue units" that are used to express the level of blood carotenoids and vitamin A are purely arbitrary. In this age group the normal range for carotenoids is between 7 and 10 units and for vitamin A around 15. Thus there was a marked reduction in these two fat-soluble vitamins or previtamins. The diagnosis of idiopathic pancreatic fibrosis would naturally lead to an attempt at substitution therapy, using one of the pancreatic extracts. Nutramigen is one of the casein hydrolysates, providing a mixture of protein break-down products, largely amino acids.

The stools became "almost fat free." That may have been due to the fact that the diet was low in fat content. The lowering of the red-cell count, of the hemoglobin and of the total protein points to poor protein absorption. Vitamin D

was furnished by ultraviolet irradiation on the assumption that fat soluble vitamins would not be absorbed from the gastrointestinal tract.

The differential diagnosis in an infant of this age, with the long, complete story that we have, does not allow many possibilities. The obvious diarrhea, the inability to tolerate fat, the failure to gain and the enlarged abdomen, all point to some difficulty with intestinal absorption.

Celiac disease would be rather unusual at such an early age. It is a condition seen in infants and young children, usually appearing late in the first year of life, with the typical symptoms not often being seen until the beginning of the second year. The disease is not associated with any change in duodenal enzymes. There is another type of disease associated with intolerance of starch, in which fat may be properly absorbed but starch inadequately taken care of; in such cases the amylase content of the duodenal fluid is low. That again appears in an apparently normal child after six months of life and has a strong tendency to be familial. Syphilis has been reported to have produced fibrosis in the pancreas and the condition outlined here; however, although no specific statement is made, I should guess that this was not syphilis.

DR. CASTLEMAN: The blood Hinton test was negative.

DR. ROSS: Sprue, the vitamin B deficiency disease, certainly has never been proved at this early age. Mechanical obstruction to absorption in the gastrointestinal tract and short circuiting, as in gastrocolic fistula, are possibilities, but there is no evidence for them.

Congenital stenosis of the gastrointestinal tract, with impairment of absorption, as seen in tuberculous peritonitis with obstruction to the return of lymph from the intestinal tract, would not appear in an infant this young. The books say that heavy-metal poisoning may cause obstruction to absorption. There is no evidence in this child that such poisoning had occurred.

I am forced to the diagnosis that the other hospital made — namely, idiopathic fibrosis of the pancreas. In support of this diagnosis we have the family history of one other child with pancreatic fibrosis and the second one with a suspicion of the same disease. There were absent trypsin and increasing anemia and hypoproteinemia despite the administration of large amounts of blood; in other words the child was unable to manufacture its own protein. These signs are associated mainly with the disease that we know as idiopathic fibrosis of the pancreas. The low fat absorption, as evidenced by the rather low cholesterol, carotenoids and vitamin A, certainly fits in with this picture. The variation in fluid metabolism that would result from large amounts of fluid in the loops of bowel that had been distended and were edematous may explain the low sodium. The one thing that is missing is the presence of respiratory infection. However, this child was so young that he possibly did not have time to develop the type of infection so classically seen in fibrosis of the pancreas after the first three or four months of life. Such infection can possibly be explained on the basis of inability to absorb fat-soluble vitamins, with the development of vitamin A deficiency, metaplasia of the epithelium of the respiratory tract and areas of infection. In this infant, however, there is no evidence that infection was the cause of death; quite possibly, even though physical examination and x-ray examination did not show it, Dr. Castleman may be able to point out evidence of pulmonary infection. The diagnosis of rickets, due to vitamin D deficiency, in a child this young and with so little growth is unlikely.

CLINICAL DIAGNOSES

Pancreatic fibrosis.
Otitis media.

DR. ROSS'S DIAGNOSES

Idiopathic pancreatic fibrosis.
Vitamin A deficiency.

ANATOMICAL DIAGNOSES

Idiopathic pancreatic fibrosis.
Pulmonary atelectasis, focal.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This child did have idiopathic pancreatic fibrosis. At autopsy the child was quite emaciated but well developed. The only gross finding that was easily visible was focal atelectasis of the lung, but no real areas of consolidation. The pancreas appeared somewhat smaller than normal and was extremely firm. Microscopically there was marked interlobular and interacinar fibrosis throughout the pancreas, and many of the acini and ducts were dilated and filled with mucus (Fig. 1). Some showed definite cyst formation. I know very little about the pathology of this condition and have invited Dr. Farber to come down from the Children's Hospital to tell us more about it.

DR. SIDNEY FARBER: I was able to study the organs of the sibling mentioned in the record who died at the community hospital. The patient, who had much the picture that Dr. Castleman has just

described, was a girl twenty months of age with symptoms that began shortly after birth. The pancreas showed a more extreme degree of atrophy, dilatation of the acini and ducts and fibrosis than the one under discussion here. But the one here I regard as a fairly marked example of the disease. In addition, the sibling had a widespread bronchopneumonia caused by *Staphylococcus aureus*, and there was rather marked obstruction in the upper respiratory tract caused by inspissated mucus and purulent material.

I shall describe some of the changes we saw in this and other cases of pancreatic fibrosis. The pancreas may be normal in appearance or it may show the picture of marked atrophy. The normal portions of the pancreas stand out above the level of the diseased lobules, which are depressed, representing areas of atrophy and fibrous-tissue replacement. The clinical picture, however, may be produced by a pancreas that grossly appears normal. On microscopic examination the obstruction will be found in the small acini, and such obstruction causes pancreatic achylia in as great a degree as that produced by ligation of the main pancreatic ducts.

The term "cystic fibrosis" has been used, but there are no true cysts. Obstruction develops in the acini and is caused by inspissated pancreatic secretion, which is propelled with difficulty into the ducts. This, in turn, causes atrophy of the acinar structures, coalescence of the fibrous-tissue stroma and the formation of new fibrous tissue. The thick inspissated material is what one sees when one looks at the duodenal contents, which are thickened and sticky.

If the disease has run some months, the trachea and bronchi and the upper respiratory tract may be literally blocked by this very thick mucus, to which is usually added staphylococcal infection.

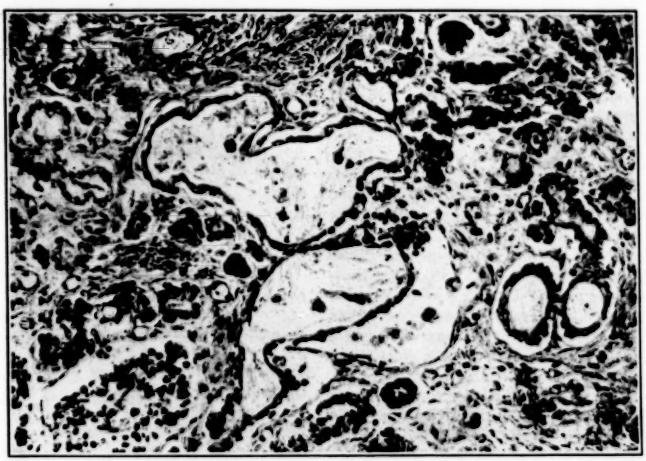

FIGURE 1. *Photomicrograph of a Section of the Pancreas.*

In this case, however, the main picture in the lung is not one of infection but rather one of obstruction. The major bronchi and the bronchioles are filled with inspissated material, and these infants may actually die of suffocation. The x-ray picture goes with these findings. Thus the same mechanism responsible for the pancreatic change appears to be responsible for the changes in the respiratory tract. Changes due to vitamin A deficiency are present in some but not all cases of this disease. Vitamin A deficiency, I believe, is not responsible for the occurrence of pulmonary infection.

The explanation for the obstruction, as well as the superimposed staphylococcal infection so often present, is found in the alteration of the character of the mucus produced by the glands of the trachea and bronchi. It is similar to the alteration found in pancreatic secretions in the pancreas. The material in the bronchial gland is thick and sticky and does not lubricate properly the mucosal surface of the trachea and bronchi. The organism

is not of great virulence as seen by the fact that little damage pathologically can be demonstrated even after the *Staph. aureus* is proved to have been present in the lung for one or two years. Similar changes may be found in the sublingual gland, duodenum, gall bladder, esophagus and bowel. One of the rare complications of the disease, which has occurred six times in our experience in recent years, is involvement of the liver in a form of cirrhosis that I have not encountered or seen described elsewhere. It is an essentially obstructive biliary cirrhosis. The bile capillaries are greatly distended and are filled with inspissated eosinophilic-staining material similar to the substance in the pancreatic acini and ducts. The obstruction causes atrophy of the liver drained by these bile capillaries and replacement fibrosis.

I have been forced to the conclusion that this disease is not a disease limited to the pancreas. The pancreas is merely one of many organs in the body affected by a general pathologic process involving secretory structures in many parts of the body. Wherever secretory structures are affected the fundamental change appears to be the same — the material secreted is more viscid, flows less readily than normal and, by mechanical action, causes obstruction to the duct system or gland system with an eventual fibrous-tissue replacement distal to the point of obstruction. There is sufficient evidence to say that vitamin A deficiency is a complication of the disease, not the cause of it. The exact cause is still unknown.

DR. CASTLEMAN: I might add that in our case there was no evidence of vitamin A deficiency. There was a small amount of mucus in the trachea and large bronchi and a very small amount in the bronchioles, which might have accounted for the focal atelectasis. There was no evidence of pneumonia. Examination of other mucous glands, such as the submaxillary gland and the duodenum, showed an early change, but nothing striking, probably because the child was so young.

CASE 29432

PRESENTATION OF CASE

A sixty-year-old woman entered the hospital because of persistent nausea and vomiting.

Eight days prior to admission the patient suffered with gaseous fullness and crampy lower abdominal pain. She passed large amounts of gas rectally, with some relief. Two days later she felt nauseated and vomited small amounts of bitter, yellow, nonbloody fluid. The nausea and intermittent vomiting continued to the day of admission, and she had been unable to retain anything except small amounts of broth. Bowel movements had been regular and normal during the illness; the patient, however, took a laxative each day. The stools were not observed to be tarry, bloody or acholic. She had not been jaundiced, nor had she suffered with fever or chills.

The patient had been admitted to the hospital seventeen months previously, at which time the left breast was radically resected because of carcinoma. The axillary lymph nodes were reported to have been uninvolved. The family history was noncontributory.

Physical examination disclosed a well-developed and well-nourished woman. There was a well-healed scar over the left chest extending into the axilla. No nodules were felt in the scar line, right breast or axillas. The heart and lungs were normal. The abdomen was distended and quite tympanitic. No tenderness was elicited, and no masses were felt. Marked peristaltic rushes were audible over the entire abdomen. Questionable dullness was percussed on the left side of the abdomen.

The blood pressure was 132 systolic, 72 diastolic. The temperature, pulse and respirations were normal.

The white-cell count was 8500. The urine was normal, and the stool guaiac negative. A Hinton test was negative. A roentgenogram of the abdomen demonstrated several loops of slightly dilated small bowel in the left midabdomen. A barium enema passed to the junction of the descending colon and sigmoid, where it met a point of practically complete obstruction. During the fluoroscopic examination no barium was seen to pass beyond the obstruction. On the films, there was a small amount of barium proximal to the lesion. There were numerous diverticulums of the sigmoid, one of which was close to the point of obstruction. On one film there appeared to be a cavity in which there was a small amount of dilute barium. There was evidence of a small pressure defect in the sigmoid just distal to the lesion. Several loops of slightly dilated small bowel were observed, and there was a large amount of gas in the cecum. The right side of the pelvis showed evidence of Paget's disease.

On the day after admission a cecostomy was established, and ten days later the barium enema was repeated. This was again unsatisfactory, since the barium did not pass the point of obstruction.

An operation was performed on the seventeenth day after admission.

DIFFERENTIAL DIAGNOSIS

DR. CLIFFORD C. FRANSEEN: It is interesting to point out that this patient had bowel movements up to the time the barium enema was done, but it was not possible to pass barium beyond the

stricture. Of course that is a frequent occurrence, — that is, barium goes easily in one direction but not in the other in this type of lesion. The x-ray pictures will undoubtedly be of great assistance, and we should see them before proceeding.

Dr. George W. Holmes: This ought to be *the* case in which the findings are due to diverticulitis.

The film of the chest is negative. Those of the abdomen show the characteristic signs of obstruction, with accumulations of gas in the small bowel. So far as the x-ray is concerned there is no positive evidence of free fluid. The diverticulums are quite large and are scattered throughout the lower sigmoid. Evidently the patient had some difficulty in retaining the enema. A retaining catheter was used, and apparently complete obstruction was demonstrated. I might add that the picture at the point of obstruction looks a little like tumor.

Dr. Franseen: Dr. Holmes says that this should be *the* case with diverticulitis, undoubtedly because we have recently discussed two cases with similar findings in which a diagnosis of diverticulitis was made only to have them both turn out to have been due to carcinoma. We shall have to review the findings to look for some evidence, other than the presence of diverticulums, for making the diagnosis of diverticulitis.

The first thing in sequence that seems to be of significance is the breast carcinoma that was operated on seventeen months previously. That is the only point in the history up to eight days before entry that gives any lead to a possible cause. The lymph nodes were uninvolved at the time of the breast operation; hence the likelihood of distant metastases is diminished, but certainly not excluded. On general principles, the first thing we ought to consider is a metastatic lesion. To my mind, a metastatic lesion that could produce this picture would be a little unusual because the obstruction to the large bowel was complete. A metastatic lesion is usually extrinsic, and would have to be extensive to produce complete obstruction by pressure on the large bowel. One could assume that there was some obstruction to the small bowel because of the dilated loops, and it is also conceivable that a metastatic lesion could have a loop of small bowel affixed to it, thus producing enough obstruction to the sigmoid to give this picture. It would be unusual, however, to have a single isolated metastasis like this from a carcinoma of the breast without other evidence of metastatic lesions.

Other things of extrinsic origin could have produced the picture — such as endometriosis. There is no way of proving any of these diagnoses, however, and the case narrows itself down in large part, if one uses the statistical method of diagnosis, to a primary lesion in the bowel.

The two most likely diagnoses are carcinoma and diverticulitis, or both. Numerically, carcinoma is, of course, the most frequent. One thing that is against carcinoma is the lack of previous trouble. On the other hand, the short history is in favor of an inflammatory lesion in an area of diverticulosis. The absence of bleeding, although favoring diverticulitis, does not entirely exclude carcinoma. It is unusual, however, for a carcinoma to produce obstruction without previous symptoms or without bleeding. It is also unusual, at least in my experience, to have the obstruction of a carcinoma so complete without previous symptoms. There was really no lumen to the bowel at the point of tumor, since the barium enema showed complete obstruction. The evidence in favor of diverticulitis, on the other hand, is the presence of numerous diverticulums. Perhaps a carcinoma was present that mechanically obstructed a diverticulum and set up a diverticulitis. The presence of a small cavity is certainly evidence in favor of an inflammatory lesion — presumably an abscess draining into the bowel, since it was shown by barium enema. If one is going to bring the small bowel into the picture I cannot escape the impression that the x-ray findings there were entirely due to backing up of gas in the small bowel. The obstruction could also have been due to secondary ileus from an inflammatory lesion. Adhesion of a loop of small bowel to the sigmoid does occur, and it is more likely to occur in an inflammatory lesion than in carcinoma. In the late stages of carcinoma of the sigmoid, of course, it frequently happens. Another thing against an inflammatory lesion is that no tenderness was elicited on examination. One would expect some tenderness in a case of diverticulitis so severe that the bowel is obstructed; but this patient was sixty years old and we know that old people can have severe inflammatory lesions in the bowel with no tenderness or spasm to account for them. The temperature, pulse and respirations were also normal, which argues to some extent against an inflammatory process, but not entirely. The white-cell count was also normal.

I end up with an uncertain picture for either carcinoma or diverticulitis. It might, of course, be both, but on the basis of the evidence presented by the x-ray findings, by the history and by the other points that I have discussed, I believe that one should go on the basis of probabilities and put diverticulitis first, with strong reservation so far as carcinoma is concerned.

DR. FLETCHER H. COLBY: Does the fact that ten days after cecostomy complete obstruction was still present favor an inflammatory lesion?

DR. FRANSEEN: Not entirely. I am sure Dr. Smithwick will agree that after cecostomy is done for an obstructing carcinoma in the lower bowel the patient frequently has spontaneous bowel movements, the lumen opening up again. To my mind, your point argues in favor of diverticulitis.

DR. REGINALD H. SMITHWICK: In my personal experience it is rather unusual for diverticulitis to produce total and persistent complete obstruction. In the 65 patients on whom we have operated in this hospital in fifteen years, there are only 4 or 5 that really had complete obstruction by barium enema when they entered the hospital. In these the obstruction cleared up completely within two weeks after proximal decompression, so that my feeling is that if obstruction fails to let up it is more in favor of cancer than it is of diverticulitis.

DR. FRANSEEN: The one strong point in favor of carcinoma is the suggestion of protrusion of a mass into the lumen of the bowel.

DR. SMITHWICK: Another point is the location of the lesion in a case such as this. It is quite difficult to say by barium enema where the descending colon ends and where the sigmoid begins, but it is rare to have any surgical complication of diverticulitis above the upper end of the sigmoid. In this particular case it is probable that the point of obstruction was in the descending colon rather than in the sigmoid. That also is in favor of cancer.

At the time of operation we were unable to tell whether this woman had diverticulitis or cancer, or both. She did have an inflammatory process and obvious diverticulums. The involved area was resected.

CLINICAL DIAGNOSIS

Carcinoma of sigmoid?
Diverticulitis with obstruction?

DR. FRANSEEN'S DIAGNOSIS

Diverticulitis of sigmoid?
Carcinoma of sigmoid?

ANATOMICAL DIAGNOSES

Adenocarcinoma of descending colon.
Diverticulosis coli.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The lesion in this case was a completely annular, constricting carcinoma, as well as multiple diverticulums. The diverticulums were distal to the cancer. I should say that the cancer was in the lower end of the descending colon rather than in the sigmoid.

DR. SMITHWICK: I cannot conceive how this patient could have gone up to a few days of the time of her hospital entry without any symptoms.

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The Journal does not hold itself responsible for statements made by any contributor.

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MEDICAL ADVERTISING

In an editorial "Council Standards and Medical Advertising," which appeared in the October 9 issue of the *Journal of the American Medical Association*, it is stated that the business managers of various state medical journals are urging the breakdown of standards set by the Council on Pharmacy and Chemistry of the American Medical Association. Since the *Journal* is one of the periodicals mentioned by name, refutation of the accusation seems justifiable.

For many years the *Journal* has obtained the majority of its contracts covering nationally advertised products from the Cooperative Medical Advertising Bureau, which was created in 1913 by the Board of Trustees of the American Medical Association. All accounts are handled through the office of the Bureau in Chicago, and this service is paid for on a commission basis. Since the Bureau is a nonprofit organization, a generous refund is made to the *Journal* at the end of each fiscal year. As part of the agreement, the *Journal* agrees to limit advertising to pharmaceutic products that have been accepted by the Council on Pharmacy and Chemistry of the American Medical Association, and failure to abide by this clause has provoked the serious accusation referred to above.

The *Journal*, at the moment, has advertising contracts with two local firms that manufacture nonaccepted products. In each instance, the drugs had never been submitted to the Council for approval, and careful investigation revealed that they were being used and recommended by authoritative physicians; furthermore, no unwarranted claims have been made in the advertising copy. All this has been done with the full knowledge of the Cooperative Medical Advertising Bureau, which, incidentally, has failed to reply to a letter dated August 11, 1943, in which it was stated that the *Journal* intended to continue with the advertising of this type unless specifically told not to do so by the Advisory Committee of the Bureau.

Another difficulty often leading inadvertently to the advertising of nonapproved drugs arises from the fact that Bureau-sponsored firms often submit copy covering such products directly to the medical journal. Unless the business manager is alert, such copy is likely to be accepted routinely.

By and large, there appears to be no concerted effort to break down, or even weaken, the standards of the Council on Pharmacy and Chemistry. Certainly there is little excuse for the statement, "The time should long since have passed when leaders of medical organizations consent to permit the exploiters of unestablished proprietary remedies to pay the bulk of printing and publishing bills of the medical journals that are supposed to

represent scientific medicine," or for the exhortation, "Let us keep the good name unsullied; its value is far above that of jewels or gold." The editorial and business staffs of the majority of state medical journals fully appreciate the good that has been accomplished by the efforts of the Council on Pharmacy and Chemistry and have no intention of "upsetting the apple cart." On the other hand, it should be appreciated that federal regulations regarding new drugs and labeling are much stricter and much more rigidly enforced than they were thirty-five years ago; that approval by the Council of effective and valuable drugs that are widely used is often unduly delayed or withheld because of minor infringement; and that the chief revenue of the majority of state medical journals is that derived from medical advertising. Previously, only one of the three members of the Advisory Committee of the Cooperative Medical Advertising Bureau had been connected with a state medical journal. Quite recently, however, the Board of Trustees of the American Medical Association, owing to pressure brought to bear by representatives of the state journals, has appointed two additional members, both of whom are editors. It is hoped that some arrangement regarding medical advertising that is advantageous both to "scientific medicine" and to the state journals will be forthcoming.

MISSILE WOUNDS OF THE SKULL AND ITS CONTENTS

It is earnestly recommended that all physicians take the trouble to read the leading article in the August 21 issue of the *Lancet*. Entitled "Treatment of Head Wounds Due to Missiles," it is an analysis of 500 cases treated during nearly two years by a mobile neurosurgical unit of the Royal Army Medical Corps in the Middle East. The author, Major P. B. Ascroft, visited Boston last May, at which time he gave a memorable talk on the same subject before a joint open meeting of the Boston Surgical Society and the Boston Society for Neurology and Psychiatry. Those fortunate enough to have been present can scarcely forget the modesty with which he cited the extraordinary results he and his team had attained. The paper contains all that he said at that time, as well as certain other data. It is obvious that any organization that can deal with over four hundred missile wounds of the skull and its contents with a mortality of only 10.6 per cent and in addition return 71 per cent of the survivors to duty in an army geared to total war speaks with authority about its specialty.

The author and head of the unit was a trained neurosurgeon whose reputation had already been established in England before undertaking this particular assignment. Assisting him were a neurologist, Major Kremer, an anesthetist, Major Cope, and two assistant surgeons, Major Hooper and Captain Northcroft. All their reported methods and conclusions have civilian as well as military application, but certain of their points bear repetition, particularly those regarding compound fractures of the skull not sustained in battle. By categorically stating that it is better not to operate in forward areas provided the patient can reach a fully equipped base hospital within forty-eight to seventy-two hours of injury, by emphasizing the importance of a mechanical sucker and by failing to mention irrigation as a therapeutic agent in dealing with these wounds, as well as in other details of resuscitation, anesthesia, lumbar puncture and so forth, they confirm under battle conditions the opinion of a group of American neurosurgeons about the value of certain procedures relative to the time and method of dealing with civilian compound fractures of the skull, and settle a debate that has exercised this specialty for some years.

It is interesting to note also that Major Ascroft recommends the use of a plaster-of-Paris bandage as a means of securing the first dressing applied at the front, as well as to protect the patient's head. This is in line with the Russian experience as detailed by Vladimir Lebedenko, surgeon and professor at the First Moscow Medical Institute, at the meeting of the American Neurological Society

in New York last May. So far as is known, this work, equally as authoritative as that reported in the English paper, has not as yet been published. Lebedenko, however, considered this therapy of sufficient importance to bring samples of such plaster casques with him from Russia. In addition, Major Ascroft's suggestion that the plaster be also used to carry a sketch of the wound should not be lost sight of. Lebedenko's reported conclusions relative to transportation, preferable locale for operative interference and proper time of operation after injury correspond closely to those reached by Major Ascroft.

It is axiomatic that the English report should be made required reading by every member of the medical departments of the Army and Navy, even should it prove necessary to reproduce it in its entirety by photostating, mimeographing or any other suitable method. In particular, copies should be made available at once to the front-line hospitals and personnel, because the conclusions differ so fundamentally from those previously authorized for publication by the War Department, which were largely reached shortly after World War I and which have been influenced little, if t all, by advances made in traumatic civilian neurosurgery in the intervening years.

All civilian surgeons should read this paper as well. Familiarity with its contents will, among other things, do much to destroy outworn shibboleths and help the overworked local doctor speak with conviction when he advocates moving the civilian prototypes of such patients to the large medical centers. Responsibilities he neither wants nor is equipped to carry on his own shoulders will be thus shifted to surgeons with better facilities and more appropriate training—with consequent benefit to the patient, the community, the doctor and the war effort.

MEDICAL EPONYM

Hines-Brown Test

This test is described by Drs. Edgar A. Hines, Jr. (b. 1906) and George E. Brown (1885–1935) in an account entitled "A Standard Stimulus for Measuring Vasomotor Reactions: Its application in the study of hypertension," which appeared in the *Proceedings of the Staff Meetings of the Mayo Clinic* (7: 332–335, 1932). A portion of the article follows:

> The subject is placed at rest for twenty minutes and the blood pressure is taken every five minutes until a constant level is obtained. Then one hand is immersed above the wrist in ice water for twenty to thirty seconds. The temperature of the water varies from 4° to 5°C. The systolic and diastolic blood pressures immediately rise, and then return to the basal level in from one to two minutes. . . .
>
> It was found that among subjects . . . with organic forms of hypertension, the average increase of systolic and diastolic pressures was greatest for all the subjects studied. . . .

A later report on the results of this test in 571 normal and hypertensive subjects appears in the *American Heart Journal* (11: 1–9, 1936).

R. W. B.

OBITUARY

HALBERT GREENLEAF STETSON

1868–1943

On September 15, 1943, Dr. Halbert G. Stetson, of Greenfield, president of the Massachusetts Medical Society in 1931 and 1932, died at his home after more than a year of failing health, occasioned by a decompensated heart. Born in Greenfield on May 8, 1868, he was educated in the public schools of Orange and at New Salem Academy, acquiring his medical education at the College of Physicians and Surgeons of Baltimore, from which he graduated in 1895. He immediately began practice in Greenfield, which he continued to within a few months of his death, although he had done little surgery for several years.

In 1899 he formed a partnership with Drs. George P. Twitchell and Charles F. Canedy, which continued until the death of Dr. Twitchell in 1930, Dr. Canedy having died in 1925.

In 1897 he married Frances A. Gildart, of Salisbury, New Brunswick, who died in 1920. They had one son, Maurice H., now living in Kalamazoo, Michigan. In 1923 he married Anna B. MacKenzie, then head nurse at the Franklin County Hospital, who survives him.

His medical affiliations included membership in the American Medical Association, Massachusetts Medical Society, American College of Surgeons, Connecticut River Valley Medical Association, and New England and New York Association of Railway Surgeons.

Although surgeon for the Boston and Maine Railroad since 1903 and medical examiner of Franklin County since 1921, his chief interest was in the Franklin County Hospital, of which he was chairman of the Board of Trustees. He had much to do with the building and development of the present hospital, which was completed in 1910, and in 1938 donated a library in honor of his former partners, Drs. Twitchell and Canedy. This was named "The Stetson Library," by the hospital staff and a bronze plaque was placed on the wall in his honor. In addition he had served in several civic capacities, including president of the Greenfield Chamber of Commerce and chairman of the School Committee.

His chief hobbies, aside from the hospital, comprised books and postcards and attendance at medical meetings.

Dr. Stetson was a man of strong character and had the respect of all who knew him.

A. H. E.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER, 1943

Résumé

Diseases	September 1943	September 1942	Seven-Year Median
Anterior poliomyelitis	122	9	14
Chicken pox	114	105	84
Diphtheria	15	9	9
Dog bite	901	846	918
Dysentery, bacillary	23	6	17
German measles	59	68	22
Gonorrhea	430	521	510
Measles	189	150	138
Meningitis, meningococcal	51	6	4
Meningitis, other forms	7	3	*
Meningitis, undetermined	3	0	*
Mumps	150	248	144
Pneumonia, lobar	114	192	120
Salmonella infections	30	33	5
Scarlet fever	397	315	168
Syphilis	482	460	427
Tuberculosis, pulmonary	217	252	239
Tuberculosis, other forms	27	12	23
Typhoid fever	2	3	9
Undulant fever	2	4	4
Whooping cough	301	778	546

*Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

Comment

The increase in poliomyelitis cases commented on in the August report has been considerably accelerated during September. The number of cases for this month was approximately nine times the seven-year median. This figure, nevertheless, is not high if judged by previous standards, and this year's outbreak on the whole will probably rank as a relatively minor one.

Meningococcal meningitis is still at a high level, nearly thirteen times the seven-year median, and there was a moderate rise over last month's figure. This may indicate that the high prevalence may continue into the next season.

Diphtheria shows a slight increase this month, owing to 8 cases in a small town that has done little immunizing for the past few years.

Scarlet fever did not drop to the usual low seasonal level. This is the twenty-fourth consecutive month in which the number of cases exceeded the number reported the same month the previous year.

Geographical Distribution of Certain Diseases

Anterior poliomyelitis was reported from: Attleboro, 2; Bedford, 1; Belmont, 3; Berkley, 1; Beverly, 23; Boston, 7; Braintree, 3; Brockton, 2; Cambridge, 1; Fall River, 6; Framingham, 1; Hinsdale, 2; Holliston, 1; Holyoke, 1; Hopkinton, 1; Lee, 2; Lynn, 11; Malden, 1; Mansfield, 1; Marblehead, 1; Maynard, 1; Medford, 1; Melrose, 1; Milton, 1; Natick, 1; Newton, 1; North Attleboro, 1; North Brookfield, 1; Norton, 1; Norwood, 2; Peabody, 2; Pittsfield, 3; Quincy, 2; Reading, 1; Revere, 1; Salem, 8; South Hadley, 1; Somerville, 1; Southbridge, 3; Springfield, 1; Swampscott, 1; Truro, 1; Wakefield, 2; Waltham, 4; Watertown, 3; Wenham, 2; Weston, 1; Weymouth, 1; Wilbraham, 1; Worcester, 1; total, 122.

Diphtheria was reported from: Arlington, 1; Blackstone, 1; Boston, 1; Boxboro, 8; Easthampton, 1; Taunton, 1; Weymouth, 1; Woburn, 1; total, 15.

Dysentery, bacillary, was reported from: Becket, 2; Boston, 2; Lawrence, 1; Malden, 1; Holyoke, 4; Melrose, 2; Northampton, 4; Wellesley, 1; Wilbraham, 1; Woburn, 5; total, 23.

Encephalitis, infectious, was reported from: Amherst, 1; Lynn, 1; Malden, 1; Stoughton, 1; total, 4.

Malaria was reported from: Amherst, 1; Camp Edwards, 1; Chelsea, 1; Fort Banks, 8; Leominster, 1; Revere, 1; Springfield, 1; total, 14.

Meningitis, meningococcal, was reported from: Acushnet, 1; Barnstable, 3; Boston, 14; Brookline, 1; Camp Edwards, 1; Chelsea Naval Hospital, 2; Dudley, 1; Fall River, 2; Fort Devens, 3; Hanover, 1; Holyoke, 1; Lowell, 3; Lynn, 1; Malden, 1; Northbridge, 1; Norfolk, 1; Revere, 1; Somerset, 1; Somerville, 2; Southbridge, 1; Wareham, 1; Westfield, 1; Weymouth, 1; Winthrop, 1; Worcester, 5; total, 51.

Meningitis, other forms, was reported from: Fall River, 1; Lawrence, 1; Lynn, 1; New Bedford, 1; Springfield, 1; Wilbraham, 1; Worcester, 1; total, 7.

Meningitis, undetermined, was reported from: Gloucester, 1; Medford, 1; Worcester, 1; total, 3.

Salmonella infections were reported from: Becket, 1; Beverly, 1; Brockton, 1; Cambridge, 2; Haverhill, 8; Lexington, 1; Lowell, 1; Pittsfield, 1; Somerville, 1; Templeton, 11; Wakefield, 1; Waltham, 1; total, 30.

Septic sore throat was reported from: Boston, 1; Marion, 4; Milton, 1; West Springfield, 1; total, 7.

Tetanus was reported from: Billerica, 1; Boston, 1; Haverhill, 1; Lowell, 1; Peabody, 1; total, 5.

Trachoma was reported from Hudson, 1; total, 1.

Trichinosis was reported from: Boston, 1; Westwood, 1; total, 2.

Typhoid fever was reported from: Gardner, 1; Malden, 1; total, 2.

Undulant fever was reported from: Adams, 1; North Brookfield, 1; total, 2.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

Clinic	Date	Clinic Consultant
Salem	November 1	Paul W. Hugenberger
Haverhill	November 3	William T. Green
Lowell	November 5	Albert H. Brewster
Pittsfield	November 15	Frank A. Slowick
Springfield	November 17	Garry deN. Hough, Jr.
Brockton	November 18*	George W. Van Gorder
Worcester	November 19	John T. O'Meara
Fall River	November 22	Eugene A. McCarthy
Hyannis	November 23	Paul L. Norton

*Date changed because of holiday.

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WAR ACTIVITIES

CIVILIAN DEFENSE

The following notice was recently released by Dr. George Baehr, chief medical officer of the Office of Civilian Defense, Washington, D. C.:

> Rumors that civilian defense is no longer necessary have recently been spread by irresponsible persons. These rumors are thoughtless or calculatingly subversive, for they are not supported by Army authorities responsible for our coastal defenses or by the present military situation.
>
> Fortunately, the success of our armed forces overseas has saved us thus far from experiencing the horrors of enemy bombing to which the cities of our allies are being subjected. In the opinion of the best military authorities our coastal areas and industrial centers will not be free of the danger of enemy attack from the air or of widespread sabotage until the *last day* of the war.
>
> Civilian defense is needed also as one of the essential measures for safeguarding internal security. This is especially true of the Emergency Medical Service. If we had not created a nationwide organization for civilian defense two years ago, we would be obliged to organize one today for home security. Disasters of all kinds have increased because of the tremendous speeding up of our great industries, the overburdening of our railroads and the inexperience of hundreds of thousands of new war workers. Our police and fire departments, our public-works and utility services and our hospitals, on which we depend for protection, are being increasingly depleted of trained personnel. We must therefore strengthen our voluntary protective services throughout the land. Along the Pacific and the Atlantic coasts these services must be especially strong in volunteer personnel and equipment to guard us against the hazards of enemy attack and sabotage until that day when the Army advises us that the danger is ended.

MISCELLANY

FIFTIETH ANNIVERSARY OF TUFTS COLLEGE MEDICAL SCHOOL

The grand assembly of the Fiftieth Anniversary of Tufts College Medical School was held on October 6 in Boston and was attended by 940 medical alumni and students. Among the speakers were Harold E. Sweet, president of the Board of Trustees of Tufts College, Dr. Alonzo K. Paine, professor of obstetrics, Dr. Karl T. Compton, president of the Massachusetts Institute of Technology, Captain A. Warren Stearns (MC), U.S.N.R., dean-on-leave, Dr. Louis E. Phaneuf, professor of gynecology, Commander Bartholomew W. Hogan (MC), U.S.N., and Dr. Leonard Carmichael, president of Tufts College.

President Carmichael read a letter that he had received from President Roosevelt, in which the accomplishments of the medical school during the fifty years subsequent to its founding were praised and well-wishes for the coming years were given. He announced that $746,000 has been raised toward the $850,000 Building-Fund goal. He also acknowledged a contribution of $125,000 by Edward Cohen toward the Building Fund. The total was exclusive of contributions that were made for various other specific purposes in connection with the medical school.

The Fiftieth Anniversary Committee consisted of Dr. Phaneuf, chairman, Dr. Carmichael, Capt. Stearns, Dr. Dwight O'Hara, acting dean, and Dr. Harry Blotner, secretary-treasurer of the Tufts Medical Alumni Association.

RENEWAL OF AWARD TO SHARP AND DOHME

Sharp and Dohme, originators of the process by which dried blood plasma is made, and sole manufacturers of the first nine-months' supply of this vital material for the armed services, was awarded the Production Army–Navy "E" for the second time on Saturday, October 16. In a letter to the workers at the Philadelphia plant and the Glenolden laboratories of Sharp and Dohme, Robert P. Patterson, Under-Secretary of War, stated: "You have continued to maintain the high standards that you set for yourselves six months ago. . . . The White Star, which the renewal adds to your Army–Navy Production Award flag, is the symbol of appreciation from our armed forces for your continued and determined effort and patriotism." Sharp and Dohme's pioneer work in developing the methods and equipment necessary for the production of dried plasma is one of the most important contributions of the biological industry and has already resulted in great saving of life through transfusion of plasma at the scene of battle.

NOTES

Dr. Joe V. Meigs has recently been appointed surgeon in charge of gynecology at the Palmer Memorial Unit of the New England Deaconess Hospital. The Gynecologic Tumor Clinic of the Out Patient Department, which for many years had been under the direction of the late Dr. G. A. Leland, Jr., will be under the guidance of Dr. Meigs.

Dr. Charles F. McKhann has recently accepted the position as assistant to the president of Parke, Davis and Company and will devote his entire time to the scientific activities of the company. From 1936 to 1940, Dr. McKhann was associate professor of pediatrics and communicable diseases at the Harvard Medical School and a member of the staff of the Children's Hospital; he then

joined the faculty of the University of Michigan, serving as professor of pediatrics and communicable diseases at the Medical School and as professor of maternal and child health at the School of Public Health.

CORRESPONDENCE

PLUMMER–VINSON SYNDROME

To the Editor: In your leader on the Plummer–Vinson Syndrome in your issue for July 22 you suggest that Kelly's name should be added to that of Paterson in discussing the upper-dysphagia-with-anemia syndrome. My reason for not mentioning Kelly is the same as my reason for no longer mentioning Plummer and Vinson. Paterson's first description of the condition was published in the *British Medical Journal* in 1906 (2:355) — thirteen years before his fuller description mentioned by you and before Kelly's. The priority is therefore quite clearly Paterson's and not Kelly's.

ARTHUR HURST

Red Gables
Headington, Oxford, England

DEPRIVATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held on October 6, the Board voted to revoke the license to practice medicine in Massachusetts of Dr. Manford R. Spalding, 129 Central Street, Auburn.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

BOOK REVIEWS

Athletic Injuries: Prevention, diagnosis and treatment. By Augustus Thorndike, M.D. Second edition. 8°, cloth, 216 pp., with 105 illustrations. Philadelphia: Lea and Febiger, 1942. $3.00.

The second edition of this book has been thoroughly revised in the light of recent advances in the physiology of physical fitness, and the chapter on physical therapy has been rewritten with the assistance of Dr. Arthur L. Watkins. The manual should be popular with all those having to do with sports and physical culture. It is well printed, with a good type, and is of handy size.

The Clinical Application of the Rorschach Test. By Ruth Bochner, M.A., and Florence Halpern, M.A. With an introduction by Karl M. Bowman, M.D. 8°, cloth, 216 pp., with 3 graphs. New York: Grune and Stratton, 1942. $3.00.

This comparatively new test is now widely used by psychiatrists. The test itself is simple in that the subject reports his interpretation of ten standardized ink blocks, pointing out everything that is revealed in or suggested by the outline of the figures. The results are then interpreted, a fairly complicated procedure only to be comprehended after considerable study under expert guidance. The aim of the test is to study the personality traits in the individual. This can, naturally, be done by prolonged personal investigation, but the time will be greatly shortened if the Rorschach test proves to be valuable. At present the test should be left in the hands of those most competent to carry it out, since it is not something that can be widely applied by unskilled workers. This book will help anyone to understand the test as it is done by the authors, both of them qualified psychologists formerly associated with the Bellevue Psychiatric Hospital.

The test itself cannot be regarded as infallible and there are still many controversial points about its value. It has, however, established itself, probably permanently, in the psychiatric clinics as an important test for personality. This book, giving the known facts regarding the test and its interpretation, is an important addition to the current literature. A number of typographical errors need correction.

Synopsis of Materia Medica, Toxicology and Pharmacology. By Forrest R. Davison, M.Sc., Ph.D., M.B. Second edition. 12°, cloth, 695 pp., with 45 illustrations. St. Louis: The C. V. Mosby Company, 1942. $5.75.

The first edition of this work was published in 1940, and it has now been found necessary to publish a second edition, which has been revised to include information on a large number of new drugs. The general plan of the work has not been changed, but in nearly every section important additions and deletions have been made. The revision conforms to the latest edition of the *National Formulary*, the twelfth edition of the *Pharmacopoeia of the United States* and the *British Pharmacopoeia*. The chapter on sulfonamide drugs has, of necessity, been enlarged.

An attempt has been made to keep the volume moderate in size, and this has led, unfortunately, to the use of a rather small type. The book also has been printed on coated stock, which makes it rather heavy for its size; a lighter paper would have made the volume easier to handle.

Memorable Days in Medicine: A calendar of biology and medicine. By Paul F. Clark, Ph.D., and Alice S. Clark. 12°, cloth, 305 pp., with 29 illustrations. Madison, Wisconsin: The University of Wisconsin Press, 1942. $2.00.

This calendar of birth and death dates of noted men in the field of biology and medicine is a useful compilation, especially for those who have to plan regular exhibits for public display. The selection is purely a personal one of the authors and therefore will not meet the ideas of all those interested in the history of medicine. It seems incongruous to include the birthdays of the Virgin Mary and Leif Ericson.

One inaccurate entry is of considerable local interest. Under date of November 27, 1782, it is stated that the Harvard Medical School was established by the Corporation of Harvard College and that three professorships were then voted to John Warren, Benjamin Waterhouse and Aaron Dexter. The records of the Corporation show that on September 19, 1782, a report embodying a plan for the formation of a medical school was adopted, and that on November 22 one professor was appointed, namely, John Warren, who managed all branches of the new school. Benjamin Waterhouse was elected on December 24, 1782, and Aaron Dexter was not voted in until May 22, 1783. It was not until October 7, 1783, that Warren and Waterhouse were inducted into office with much ceremony.